P2RY8 ANTIBODIES AND METHODS OF TREATING CANCER

FIELD OF THE DISCLOSURE

[0001] The present disclosure relates, in general, to antibodies specific for P2RY8 and uses thereof to treat cancer.

CROSS-REFERENCE TO RELATED APPLICATIONS

[0002] This application claims the benefit of U.S. Provisional Application No. 63/600,437, filed on November 17, 2023, the entire contents of which are incorporated herein in their entirety by this reference.

BACKGROUND

[0003] Antibodies constitute powerful therapeutic agents characterized by limited side effects due to their ability to specifically target a distinct antigen on a cell, bacteria, virus, or toxin in connection with P2RY8-associated disease such as lymphomas. There is a clinical need to provide new, additional antibodies, such as the antibodies described herein to address the medical needs of patients relating to lymphomas.

SUMMARY

[0004] Provided herein are antigen-binding proteins which bind to P2RY8 protein. In various aspects, the antigen-binding protein of the present disclosure binds to a human P2RY8 protein (UniProt accession number: Q86VZ1; SEQ ID NO: 369) and optionally binds to a monkey P2RY8 protein but not bind substantially to dog P2RY8 protein (NCBI RefSeq accession number: XP_013967130.1; SEQ ID NO: 371). In various aspects, the antigen-binding protein binds to the extracellular domain (ECD) of P2RY8 protein. In various embodiments, the disclosure provides an antigen binding protein against P2RY8 protein.

[0005] In various aspects, the antigen binding protein binds to P2RY8 endogenously expressed by human cancer cells, e.g., lymphoma cells. In various instances, the antigen-binding proteins of the present disclosure inhibit tumor growth in a subject, e.g., a human, without any other moiety attached to the antigen-binding protein (e.g., naked antigen-binding protein). In various instances, the naked antigen-binding proteins inhibit tumor growth in a subject, e.g., a human.

[0006] Without being bound to a particular theory, the anti-tumor activities of the antigen-binding proteins provided herein allow such entities to be useful in methods of reducing tumor growth and treating a subject with a tumor or cancer. As further discussed herein, in various aspects, the antigen-binding protein encompasses an antibody, antigen-

binding antibody fragment thereof, or antibody protein product (e.g., engineered protein comprising an antibody or a fragment thereof).

[0007] The present disclosure also provides antigen-binding proteins comprising at least 3, 4, 5, or all amino acid sequences of a specified group of amino acid sequences. In various aspects, the antigen-binding proteins comprise at least 3, 4, 5, or 6 complementary determining region (CDR) amino acid sequences of P2RY8 antibodies disclosed herein.

[0008] The present disclosure further provides antigen-binding proteins comprising amino acid sequences as detailed herein.

[0009] The present disclosure provides a bispecific antigen-binding protein that binds to P2RY8 protein and a second antigen. The bispecific antigen-binding protein may comprise any one of the antigen-binding protein described here. The second antigen may be a cell surface protein, optionally a protein whose binding modulates immune response. The bispecific antigen-binding protein may take any structure, e.g., diabody, TandAb (tandem diabody), BiTE (bispecific T cell engager), etc.

[0010] The present disclosure also provides a conjugate that comprises an antigen-binding protein or a bispecific antigen-binding protein and a heterologous moiety (e.g., a cytotoxic drug). The conjugate may comprise a cleavable linker or a non-cleavable linker. The conjugate may have various number of a heterologous moiety (an agent) conjugated to an antigen-binding protein or a bispecific antigen-binding protein described herein, preferably 1-8 agents per protein or 3-8 agents per protein. Alternatively, the conjugate may have various number of two or more heterologous moieties (e.g., two or more different agents) conjugated to an antigen-binding protein or a bispecific antigen-binding protein. The conjugate may be a site-specific conjugate. The conjugate may be a homogenous conjugate or a heterogeneous conjugate.

[0011] In certain aspects, the antigen-binding proteins of the present disclosure may comprise a tag (e.g., HA, myc, flag, GST) and/or may be detectably labeled (e.g., comprising GFP, conjugated to a fluorescent agent, labeled with a radioisotope, attached to an enzyme (e.g., luciferase), etc.).

[0012] Related polypeptides, nucleic acids, vectors, host cells, and conjugates are further provided herein. Kits and pharmaceutical compositions comprising such entities are moreover contemplated.

[0013] Also provided are methods of making an antigen-binding protein. In various embodiments, the method comprises culturing a host cell comprising a nucleic acid

encoding an antigen-binding protein or a polypeptide as described herein so as to express the antigen-binding protein or polypeptide.

[0014] Methods of treating a subject having cancer are additionally provided herein. In various embodiments, the method comprises administering to the subject a pharmaceutical composition of the present disclosure in an amount effective for treating cancer in the subject.

[0015] Also provided are methods of treating a subject with a P2RY8-expressing cancer comprising administering to the subject a pharmaceutical composition described herein. In various embodiments, the P2RY8-expressing cancer expresses P2RY8 protein. The P2RY8-expressing cancer cell may overexpress wild-type P2RY8 protein, express a mutant P2RY8 protein or express a fusion of a P2RY8 protein. Further contemplated is a method of inhibiting tumor growth in a subject, comprising administering to the subject a pharmaceutical composition described herein.

[0016] A method of reducing tumor size in a subject or preventing the recurrence of cancer in a subject comprising administering to the subject a pharmaceutical composition are described and provided herein.

[0017] Also provided herein is a method of treating cancer in a subject diagnosed to be an over-expresser of P2RY8 protein, comprising administering to the subject a pharmaceutical composition described herein.

[0018] In various embodiments, the administering step induces apoptosis in tumor cells, for example in cells expressing P2RY8 protein. In various embodiments, the administration induces antibody-dependent cell-mediated cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC), tumor necrosis and death or depletion of cells, and/or disruption of tumor cell adherence, each of which aids in tumor regression or slowing of tumor growth.

BRIEF DESCRIPTION OF THE DRAWINGS

[0019] **FIG. 1** is a box plot of P2RY8 expression in normal human tissues or cells from GTEx data, GTEx_Analysis_2017-06-05_v8_RNASeQCv1.1.9_gene_tpm, downloaded from GTEx portal (World Wide Web at gtexportal.org/home/datasets) and plotted with ggplot2 package in R programing language.

[0020] **FIG. 2** is a box plot of P2RY8 expression in human cancer from TCGA. P2RY8 RNA expression data from a total of 10,071 human cancer tissue samples were downloaded from cBioPortal (World Wide Web at cbioportal.org/) and plotted with ggplot2 package in R programing language.

[0021] **FIG. 3** is a box plot of P2RY8 expression in TORL human cancer cell line panel. A total of 587 human cancer cell lines were analyzed for P2RY8 RNA expression.

[0022] **FIG. 4** is a sequence alignment of human P2RY8 protein (UniProt accession number: Q86VZ1; SEQ ID NO: 369), crab-eating Macaque (*Macaca fascicularis*) P2RY8 protein (NCI Ref Seq: XP_005595888.1; SEQ ID NO: 370), and dog P2RY8 protein (NCBI Ref Seq: XP_013967130.1; SEQ ID NO: 371), using Clustal Omega multi-sequence alignment program (Sievers F., et al., (2011): Mol. Syst. Biol. 7:539).

[0023] **FIG. 5A-FIG. 5C** show efficacy of P2RY8 mouse mAbs in P2RY8-positive lymphoma cell line xenografts. Fig. 5A-Fig. 5C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 5**A**) or mean change in tumor volume (mm^3) at Day 24 (Fig. 5**B**) of tumors and percent change in body weight (Fig. 5**C**) in SCID mice bearing a human P2RY8-positive B cell lymphoma cell line, SU-DHL-5 (ATCC CRL-2958), after treatment weekly at 10 mg/kg with control human IgG1 antibody (Hu-IgG) or 5 different chimeric anti-P2RY8 antibodies (P2RY8 mAb-690, P2RY8 mAb-716, P2RY8 mAb-720, P2RY8 mAb-724, or P2RY8 mAb-729) directed against P2RY8 protein. Each chimeric anti-P2RY8 antibody comprises a mouse immunoglobulin (Ig) heavy and light chain variable regions (V_H and V_L) and a human Ig gamma 1 (IgG1) heavy chain constant region and a human kappa (κ) light chain constant region. Treatment every 4 days at 10 mg/kg with Rituximab (anti-CD20 chimeric antibody against B cell lymphoma) is provided for comparison.

[0024] **FIG. 6A-FIG. 6C** show efficacy of P2RY8 mouse mAbs in P2RY8-positive lymphoma cell line xenografts. Fig. 6A-Fig. 6C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 6**A**) or mean change in tumor volume (mm^3) at Day 15 (Fig. 6**B**) of tumors and percent change in body weight (Fig. 6**C**) in SCID mice bearing a different human P2RY8-positive B cell lymphoma cell line, SU-DHL-10, (ATCC CRL-2963), after treatment weekly at 10 mg/kg with control human IgG1 antibody (Hu-IgG) or 5 different chimeric P2RY8 antibodies (P2RY8 mAb-690 (also referred to herein as 10-0690-m), P2RY8 mAb-716 (also referred to herein as 10-0716-m or P2RY8mAb-716), P2RY8 mAb-720 (also referred to herein as 10-0720-m), P2RY8 mAb-724 (also referred to herein as 10-0724-m), or P2RY8 mAb-729 (also referred to herein as 10-0729-m)) directed against P2RY8 protein. Treatment every 4 days at 10 mg/kg with Rituximab (anti-CD20 chimeric antibody against B cell lymphoma) is provided for comparison.

[0025] **FIG. 7A-FIG. 7C** show that P2RY8 mouse mAbs have no activity in P2RY8-negative lymphoma cell line xenografts. Fig. 7A-Fig. 7C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 7**A**) or mean change in tumor volume (mm^3) at Day 23 (Fig. 7**B**) of tumors and percent change in body weight (Fig. 7**C**) in SCID mice bearing human P2RY8-negative B-cell non-Hodgkin lymphoma cell line (SCC-3; RRID: CVCL_1683) after treatment weekly at 10 mg/kg with control human IgG1 antibody (Hu-IgG) or 5 different chimeric P2RY8 antibodies (P2RY8 mAb-690, P2RY8 mAb-716, P2RY8 mAb-720, P2RY8 mAb-724, or P2RY8 mAb-729) directed against P2RY8 protein. Treatment every 4 days at 10 mg/kg with Rituximab (anti-CD20 chimeric antibody against B cell lymphoma) is provided for comparison.

[0026] **FIG. 8** shows staining of a P2RY8-positive human large B-cell lymphoma cell line, Karpas-1106P (RRID: CVCL_1821), with four candidate humanized anti-P2RY8 antibodies (716-h3 (also referred to herein as P2RY8 mAb-716-h3), 716-h4 (also referred to herein as P2RY8 mAb-716-h4), 716-h5 (also referred to herein as P2RY8 mAb-716-h5) or 716-h6 (also referred to herein as P2RY8 mAb-716-h6) in an indirect immunofluorescence assay with Alexa Fluor® 647 (AF647)-labeled rat anti-human IgG Fc secondary IgG2a antibody in top panels and phase contrast images of the same field of cells in corresponding bottom panels. Scale bar = 50 μm

[0027] **FIG. 9** shows staining of a P2RY8-positive human large B-cell lymphoma cell line, Karpas-1106P (RRID: CVCL_1821), with three additional candidate humanized anti-P2RY8 antibodies, 716-h7, 716-h8 (also referred to herein as P2RY8 mAb-716-h8) and 716-h9 or a chimeric anti-P2RY8 antibody 716-m (also referred to herein as P2RY8 mAb-716) shown in an indirect immunofluorescence assay with AF647-labeled rat anti-human IgG-Fc secondary IgG2a antibody in top panels and phase contrast images of the same of cells in corresponding bottom panels. Scale bar = 50 μm

[0028] **FIG. 10A-FIG. 10C** represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 10**A**) or mean change in tumor volume (mm^3) at Day 20 (Fig. 10**B**) of tumors and percent change in body weight (Fig. 10**C**) in SCID mice bearing human P2RY8-positive large B cell lymphoma cell line, SU-DHL-5 (ATCC CRL-2958), after treatment weekly at 10 mg/kg with control human IgG1 antibody (Hu-IgG), one chimeric anti-P2RY8 antibody (P2RY8 mAb-716) or four different humanized anti-P2RY8 antibodies (P2RY8 mAb-716-h3, P2RY8 mAb-716-h4, P2RY8 mAb-716-h5, or P2RY8 mAb-716-h6) of P2RY8 mAb-716 antibody. The P2RY8 mAb-716-h3 to h6 humanized

antibodies are human IgG1-kappa (IgG1κ) antibodies comprising the CDRs of P2RY8 mAb-716 antibody and/or its CDR variants. Treatment every 4 days at 10 mg/kg with Rituximab is provided for comparison.

[0029] **FIG. 11A-FIG. 11C** represents a graph of tumor volume (mm^3) as a function of time (days) (Fig. 11**A**) or mean change in tumor volume (mm^3) at Day 20 (Fig. 11**B**) of tumors and percent change in body weight (Fig. 11**C**) in SCID mice bearing a human P2RY8-negative B-cell non-Hodgkin lymphoma cell line, SCC-3 (RRID: CVCL_1683), after treatment weekly at 10 mg/kg with control human IgG1 antibody (Hu-IgG), one chimeric anti-P2RY8 antibody (P2RY8 mAb-716) or four different humanized anti-P2RY8 antibodies (P2RY8 mAb-716-h3, P2RY8 mAb-716-h4, P2RY8 mAb-716-h5, or P2RY8 mAb-716-h6) of P2RY8 mAb-716 antibody. Treatment every 4 days at 10 mg/kg with Rituximab is provided for comparison.

[0030] **FIG. 12** shows time course of internalization of AF647-labeled chimeric anti-P2RY8 antibody, P2RY8 mAb-716 (also referred to herein as 0716m), in a P2RY8-positive human large B-cell lymphoma cell line, Karpas-1106P (RRID: CVCL_1821), stained with Hoechst 33342 DNA dye. Fluorescence microscopy images are shown with overlay on phase contrast images shown for the bottom two panels. Scale bar = 10 μm

[0031] **FIG. 13** shows time course of internalization of AF647-labeled chimeric anti-P2RY8 antibody, P2RY8 mAb-716 (also referred to herein as 0716m), in a P2RY8-positive human large B-cell lymphoma cell line, Karpas-1106P (RRID: CVCL_1821). Fluorescence microscopy image is shown with overlay on a phase contrast image shown for the last time point (bottom panel). Scale bar = 10 μm

[0032] **FIG. 14** shows time course of internalization of AF647-labeled chimeric anti-P2RY8 antibody, P2RY8 mAb-716 (also referred to herein as 0716m), in a P2RY8-positive human large B-cell lymphoma cell line, SU-DHL-5 (ATCC CRL-2958). Fluorescence microscopy image is shown with overlay on a phase contrast image shown for the last time point (bottom panel). Scale bar = 10 μm

[0033] **FIG. 15** shows time course of internalization of AF647-labeled chimeric anti-P2RY8 antibody, P2RY8 mAb-716 (also referred to herein as 0716m), in a HEK293T cell line transfected with a human P2RY8-mGFP expression vector and stained with Hoechst 33342 DNA dye. Fluorescence microscopy images are shown: anti-P2RY8 antibody (red), P2RY8-mGFP fusion protein (green) and nucleus (blue). First panel on left shows only

AF647 fluorescence; the AF647-labeled anti-P2RY8 antibody stained the cell membrane prior to cellular internalization. Scale bar = 10 μm

[0034] **Fig. 16** shows time course of internalization of AF647-labeled humanized anti-P2RY8 antibody, P2RY8 mAb-716-h3 (also referred to herein as 716-h3), in a P2RY8-positive human large B-cell lymphoma cell line, Karpas-1106P (RRID: CVCL_1821). Fluorescence microscopy images are shown with overlay on phase contrast images shown for the four later time points. Scale bar = 10 μm

[0035] **Fig. 17A- FIG. 17C** show efficacy of P2RY8-ADC in P2RY8-positive SUDHL-10 lymphoma cell line xenografts with IVIG pre-treatment. Fig. 17A-Fig. 17C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 17**A**) or mean change in tumor volume (mm^3) at Day 23 (Fig. 17**B**) of tumors and percent change in body weight (Fig. 17**C**) in SCID mice bearing a human P2RY8-positive B cell lymphoma cell line, SU-DHL-10, (ATCC CRL-2963), after treatment weekly at 2.5 mg/kg with non-targeting human IgG1 antibody (Hu-IgG control mAb), Hu-IgG control mAb conjugated to MMAE (Hu-IgG control ADC) or a humanized P2RY8 antibody conjugated to MMAE (P2RY8-716-h3-ADC). Each mouse also received 10 mg/kg human immunoglobulin (IVIG) 24 hours before each dose of ADC or control mAb.

[0036] **Fig. 18A- FIG. 18C** show efficacy of P2RY8-ADC in P2RY8-positive SUDHL-5 lymphoma cell line xenografts with IVIG pre-treatment. Fig. 18A-Fig. 18C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 18**A**) or mean change in tumor volume (mm^3) at Day 11 (Fig. 18**B**) of tumors and percent change in body weight (Fig. 18**C**) in SCID mice bearing a human P2RY8-positive B cell lymphoma cell line, SU-DHL-5 (ATCC CRL-2958), after treatment weekly at 2.5 mg/kg with non-targeting human IgG1 antibody (Hu-IgG control mAb), Hu-IgG control mAb conjugated to MMAE (Hu-IgG control ADC) or a humanized P2RY8 antibody conjugated to MMAE (P2RY8-716-h3-ADC). Each mouse also received 10 mg/kg human immunoglobulin (IVIG) 24 hours before each dose of ADC or control mAb.

[0037] **Fig. 19A- FIG. 19C** show efficacy of P2RY8-ADC in P2RY8-positive RL lymphoma cell line xenografts. Fig. 19A-Fig. 19C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 19**A**) or mean change in tumor volume (mm^3) at Day 24 (Fig. 19**B**) of tumors and percent change in body weight (Fig. 19**C**) in SCID mice bearing a human P2RY8-positive B cell lymphoma cell line, RL (ATCC CRL-2261), after treatment weekly with 10 mg/kg of a non-targeting human IgG1 antibody (Hu-IgG control

mAb), 5 mg/kg of the Hu-IgG control mAb conjugated to MMAE (Hu-IgG control ADC) or 5 mg/kg of a humanized P2RY8 antibody conjugated to MMAE (P2RY8-716-h3-ADC).

[0038] **Fig. 20A- FIG. 20C** show lack of activity of P2RY8-ADC in P2RY8-negative SCC-3 lymphoma cell line xenografts. Fig. 20A-Fig. 20C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 20**A**) or mean change in tumor volume (mm^3) at Day 16 (Fig. 20**B**) of tumors and percent change in body weight (Fig. 20**C**) in SCID mice bearing a human P2RY8-negative B cell lymphoma cell line, SCC-3 (Cellosaurus CVCL_1683)), after treatment weekly with 10 mg/kg of a non-targeting human IgG1 antibody (Hu-IgG control mAb), 5 mg/kg of the Hu-IgG control mAb conjugated to MMAE (Hu-IgG control ADC) or 5 mg/kg of a humanized P2RY8 antibody conjugated to MMAE (P2RY8-716-h3-ADC).

[0039] **Fig. 21A- FIG. 21C** show efficacy of P2RY8-ADC in P2RY8-positive SUDHL-10 lymphoma cell line xenografts without IVIG pre-treatment. Fig. 21A-Fig. 21C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 21**A**) or mean change in tumor volume (mm^3) at Day 20 (Fig. 21**B**) of tumors and percent change in body weight (Fig. 21**C**) in SCID mice bearing a human P2RY8-positive B cell lymphoma cell line, SU-DHL-10, (ATCC CRL-2963), after treatment weekly with 10 mg/kg of a non-targeting human IgG1 antibody (Hu-IgG control mAb), 5 mg/kg of the Hu-IgG control mAb conjugated to MMAE (Hu-IgG control ADC) or 5 mg/kg of a humanized P2RY8 antibody conjugated to MMAE (P2RY8-716-h3-ADC).

[0040] **Fig. 22A- FIG. 22C** show efficacy of P2RY8-ADC in P2RY8-positive SUDHL-5 lymphoma cell line xenografts without IVIG pre-treatment. Fig. 22A-Fig. 22C represent a graph of tumor volume (mm^3) as a function of time (days) (Fig. 22**A**) or mean change in tumor volume (mm^3) at Day 20 (Fig. 22**B**) of tumors and percent change in body weight (Fig. 22**C**) in SCID mice bearing a human P2RY8-positive B cell lymphoma cell line, SU-DHL-5 (ATCC CRL-2958), after treatment weekly with 10 mg/kg of a non-targeting human IgG1 antibody (Hu-IgG control mAb), 5 mg/kg of the Hu-IgG control mAb conjugated to MMAE (Hu-IgG control ADC) or 5 mg/kg of a humanized P2RY8 antibody conjugated to MMAE (P2RY8-716-h3-ADC).

DETAILED DESCRIPTION

[0041] The present disclosure describes an antigen binding protein against P2RY8 protein, e.g., specific for P2RY8 protein, a $G\alpha_{13}$-coupled receptor, to treat P2RY8-expressing cancers.

[0042] *Antigen binding proteins*

[0043] Provided herein are antigen-binding proteins that bind to P2RY8 protein. The antigen-binding proteins of the present disclosure can take any one of many forms of antigen-binding proteins known in the art. In various embodiments, the antigen-binding proteins of the present disclosure take the form of an antibody, or antigen-binding antibody fragment, or an antibody protein product.

[0044] In various embodiments of the present disclosure, the antigen-binding protein comprises, consists essentially of, or consists of an antibody. As used herein, the term "antibody" refers to a protein having a conventional immunoglobulin format, comprising heavy and light chains, and comprising variable and constant regions. For example, an antibody may be an IgG which is a "Y-shaped" structure of two identical pairs of polypeptide chains, each pair having one "light" (typically having a molecular weight of about 25 kDa) and one "heavy" chain (typically having a molecular weight of about 50-70 kDa). An antibody has a variable region and a constant region. In IgG formats, the variable region is generally about 100-110 or more amino acids, comprises three complementarity determining regions (CDRs), is primarily responsible for antigen recognition, and substantially varies among other antibodies that bind to different antigens. The constant region allows the antibody to recruit cells and molecules of the immune system. The variable region is made of the N-terminal regions of each light chain and heavy chain, while the constant region is made of the C-terminal portions of each of the heavy and light chains. (Janeway et al., "Structure of the Antibody Molecule and the Immunoglobulin Genes", Immunobiology: The Immune System in Health and Disease, 4th ed. Elsevier Science Ltd./Garland Publishing, (1999)).

[0045] The general structure and properties of CDRs of antibodies have been described in the art. Briefly, in an antibody scaffold, the CDRs are embedded within a framework in the heavy and light chain variable region where they constitute the regions largely responsible for antigen binding and recognition. A variable region typically comprises at least three heavy or light chain CDRs (designated CDR regions 1-3, CDR1, CDR2, and CDR3 by Kabat et al., 1991, Sequences of Proteins of Immunological Interest, Public Health Service N.I.H., Bethesda, Md.; see also Chothia and Lesk, 1987, J. Mol. Biol. 196:901-917; Chothia et al., 1989, Nature 342: 877-883), within a framework region (designated framework regions 1-4, FR1, FR2, FR3, and FR4, by Kabat et al., 1991; see also Chothia and Lesk, 1987, supra). In a related embodiment, the residues of the

framework are altered. The heavy chain framework regions which can be altered lie within regions designated H-FR1, H-FR2, H-FR3 and H-FR4, which surround the heavy chain CDR residues, and the residues of the light chain framework regions which can be altered lie within the regions designated L-FR1, L-FR2, L-FR3 and L-FR4, which surround the light chain CDR residues. An amino acid within the framework region may be replaced, for example, with any suitable amino acid identified in a human framework or human consensus framework. Variable region of each light chain and heavy chain may be divided or assembled in the order: FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4.

[0046] Antibodies can comprise any constant region known in the art. Human light chains are classified as kappa and lambda light chains. Heavy chains are classified as mu, delta, gamma, alpha, or epsilon, and define the antibody's isotype as IgM, IgD, IgG, IgA, and IgE, respectively. IgG has several subclasses, including, but not limited to IgG1, IgG2, IgG3, and IgG4. IgM has subclasses, including, but not limited to, IgM1 and IgM2. Embodiments of the present disclosure include all such subclasses or isotypes of antibodies. The light chain constant region can be, for example, a kappa- or lambda-type light chain constant region, e.g., a human kappa- or lambda-type light chain constant region. The heavy chain constant region can be, for example, an alpha-, delta-, epsilon-, gamma-, or mu-type heavy chain constant regions, e.g., a human alpha-, delta-, epsilon-, gamma-, or mu-type heavy chain constant region. Accordingly, in various embodiments, the antibody is an antibody of isotype IgA, IgD, IgE, IgG, or IgM, including any one of IgG1, IgG2, IgG3 or IgG4. In a preferred embodiment, the antibody is an antibody of isotype IgG. In a preferred embodiment, the IgG1 is an antibody of subclass IgG1. In various aspects, the antibody comprises a constant region comprising one or more amino acid modifications, relative to the naturally occurring counterpart, in order to improve half-life/stability or to render the antibody more suitable for expression/manufacturability. In various instances, the antibody comprises a constant region wherein the C-terminal Lys residue that is present in the naturally occurring counterpart is removed or clipped.

[0047] The antibody can be a monoclonal antibody. In some embodiments, the antibody comprises a sequence that is substantially similar to a naturally occurring antibody produced by a mammal, e.g., mouse, rabbit, goat, horse, hamster, human, and the like. In this regard, the antibody can be considered as a mammalian antibody, e.g., a mouse antibody, rabbit antibody, goat antibody, horse antibody, hamster antibody, human antibody, and the like. In certain aspects, the antigen-binding protein is an antibody, such

as a human antibody. In certain aspects, the antigen-binding protein is a chimeric antibody or a humanized antibody. The term "chimeric antibody" refers to an antibody containing domains from two or more different antibodies. A chimeric antibody can, for example, contain the constant domains from one species and the variable domains from a second, or more generally, can contain stretches of amino acid sequence from at least two species. A chimeric antibody also can contain domains of two or more different antibodies within the same species. The term "humanized" when used in relation to antibodies refers to antibodies having at least CDR regions from a non-human source which are engineered to have a structure and immunological function more similar to true human antibodies than the original source antibodies. For example, humanizing can involve grafting a CDR from a non-human antibody, such as a mouse antibody, into a human antibody. Humanizing also can involve select amino acid substitutions to make a non-human sequence more similar to a human sequence. Information, including sequence information for human antibody heavy and light chain constant regions is publicly available through the UniProtKB database as well as other databases well-known to those in the field of antibody engineering and production. For example, the IgG1 constant region is available from the UniprotKB database as described below, incorporated herein by reference. Additionally, in another example, the human IgG2 constant region is available from the UniprotKB database as Uniprot accession number P01859, incorporated herein by reference.

[0048] Merely by way of example, the sequence for a murine immunoglobulin kappa light chain constant region or an immunoglobulin gamma-2A heavy chain constant region includes the following.

Name:	Sequence:
Immunoglobulin kappa constant, mouse (IGKC_MOUSE; UniProt ID: P01837)	RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYPKDINVKWK IDGSERQNGVLNSWTDQDSKDSTYSMSSTLTLTKDEYERHN SYTCEATHKTSTSPIVKSFNRNEC
Ig gamma-2A chain C region, A allele, mouse (GCAA_MOUSE	AKTTAPSVYPLAPVCGDTTGSSVTLGCLVKGYFPEPVTLTW NSGSLSSGVHTFPAVLQSDLYTLSSSVTVTSSTWPSQSITCN VAHPASSTKVDKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIF PPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVH

; UniProt ID: P01863)	TAQTQTHREDYNSTLRVVSALPIQHQDWMSGKEFKCKVNN KDLPAPIERTISKPKGSVRAPQVYVLPPPEEEMTKKQVTLTC MVTDFMPEDIYVEWTNNGKTELNYKNTEPVLDSDGSYFMY SKLRVEKKNWVERNSYSCSVVHEGLHNHHTTKSFSRTPGK

Merely by way of example, the sequences for human immunoglobulin kappa light chain constant (IGKC) region, human immunoglobulin lambda constant 2 light chain (IGLC2) region, human immunoglobulin gamma 1 heavy chain constant (IGHG1) region, and human immunoglobulin gamma 2 heavy chain constant (IGHG2) region include the following.

Name:	Sequence:
Immunoglobulin kappa constant, human (IGKC_HUMAN; UniProt ID: P01834)	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSS TLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
Immunoglobulin lambda constant 2, human (IGLC2_HUMAN; UniProt ID: P0DOY2)	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAV TVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLT PEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
Immunoglobulin heavy constant gamma 1, human (IGHG1_HUMAN; UniProt ID: P01857)	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQT YICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLG GPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFN WYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYK TTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEA LHNHYTQKSLSLSPGK

Immunoglobulin heavy constant gamma 2, human (IGHG2_HUMAN; Uniprot ID: P01859)	ASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVS WNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSNFGTQT YTCNVDHKPSNTKVDKTVERKCCVECPPCPAPPVAGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVQFNWYV DGVEVHNAKTKPREEQFNSTFRVVSVLTVVHQDWLNGK EYKCKVSNKGLPAPIEKTISKTKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDISVEWESNGQPENNYKTTPP MLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALH NHYTQKSLSLSPGK

[0049] An antibody can be cleaved into fragments by enzymes, such as, e.g., papain and pepsin. Papain cleaves an antibody to produce two Fab fragments and a single Fc fragment. Pepsin cleaves an antibody to produce a $F(ab')_2$ fragment and a pFc' fragment. In various aspects of the present disclosure, the antigen-binding protein of the present disclosure is an antigen-binding fragment of an antibody (a.k.a., antigen-binding antibody fragment, antigen-binding fragment, antigen-binding portion). In various instances, the antigen-binding antibody fragment is a Fab fragment or a $F(ab')_2$ fragment.

[0050] The architecture of antibodies has been exploited to create a growing range of alternative antibody formats that spans a molecular-weight range of at least about 12–150 kDa and has a valency (n) range from monomeric (n = 1), to dimeric (n = 2), to trimeric (n = 3), to tetrameric (n = 4), and potentially higher; such alternative antibody formats are referred to herein as "antibody protein products". Antibody protein products include those based on the full antibody structure and those that mimic antibody fragments which retain full antigen-binding capacity, e.g., scFvs, Fabs and VHH/VH (discussed below). The smallest antigen-binding fragment that retains its complete antigen binding site is the Fv fragment, which consists entirely of variable (V) regions. A soluble, flexible amino acid peptide linker is used to connect the V regions to a scFv (single chain fragment variable) fragment for stabilization of the molecule, or the constant (C) domains are added to the V regions to generate a Fab fragment [fragment, antigen-binding]. In exemplary aspects, the antigen binding fragment is a Fab. In exemplary aspects, the antigen binding fragment is a scFv. Both scFv and Fab fragments can be easily produced in host cells, e.g., prokaryotic host cells. Other antibody protein products include disulfide-bond stabilized scFv (ds-scFv), single chain Fab (scFab), as well as di- and multimeric antibody formats like dia-,

tria- and tetra-bodies, or minibodies (miniAbs) that comprise different formats consisting of scFvs linked to oligomerization domains. The smallest fragments are VHH/VH of camelid heavy chain Abs as well as single domain Abs (sdAb). The building block that is most frequently used to create novel antibody formats is the single-chain variable (V)-domain antibody fragment (scFv), which comprises V domains from the heavy and light chain (VH and VL domain) linked by a peptide linker of ~15 amino acid residues. A peptibody or peptide-Fc fusion is yet another antibody protein product. The structure of a peptibody consists of a biologically active peptide grafted onto an Fc domain. Peptibodies are well-described in the art. See, e.g., Shimamoto et al., mAbs 4(5): 586-591 (2012).

[0051] Other antibody protein products include a single chain antibody (SCA); a diabody; a triabody; a tetrabody; bispecific or trispecific antibodies, and the like. Bispecific antibodies can be divided into five major classes: BsIgG, appended IgG, bispecific antibody (BsAb) fragments, bispecific fusion proteins, and BsAb conjugates. See, e.g., Spiess et al., Molecular Immunology 67(2) Part A: 97-106 (2015).

[0052] In various aspects, the antigen-binding protein of the present disclosure comprises, consists essentially of, or consists of any one of these antibody protein products. In various aspects, the antigen-binding protein of the present disclosure comprises, consists essentially of, or consists of any one of an scFv, Fab VHH/VH, Fv fragment, ds-scFv, scFab, dimeric antibody, multimeric antibody (e.g., a diabody,, triabody, tetrabody), miniAb, peptibody VHH/VH of camelid heavy chain antibody, sdAb, diabody; a triabody; a tetrabody; a bispecific or trispecific antibody, BsIgG, appended IgG, BsAb fragment, bispecific fusion protein, and BsAb conjugate.

[0053] In various instances, the antigen-binding protein of the present disclosure is an antibody protein product in monomeric form, or polymeric, oligomeric, or multimeric form. In certain embodiments in which the antibody comprises two or more distinct antigen binding regions fragments, the antibody is considered bispecific, trispecific, or multi-specific, or bivalent, trivalent, or multivalent, depending on the number of distinct epitopes that are recognized and bound by the antibody.

[0054] In various embodiments, an anti-P2RY8 antibody or antibody variant thereof is selected from the group consisting of a human antibody, a humanized antibody, a chimeric antibody, a monoclonal antibody, a recombinant antibody, an antigen-binding antibody fragment, a single chain antibody, a monomeric antibody, a diabody, a triabody, a

tetrabody, a Fab fragment, an IgG1 antibody, an IgG2 antibody, an IgG3 antibody, and an IgG4 antibody.

[0055] In various aspects, the antigen-binding protein of the present disclosure is linked to a therapeutic agent. As described below, the therapeutic agent may be any known in the art, including, but not limited to, chemotherapeutic agents, cytokines and growth factors, cytotoxic agents, and the like. See "*Conjugates*" below.

[0056] *Bispecific formats*

[0057] In exemplary aspects, the antigen-binding protein is bispecific and thus capable of binding two different and distinct antigens. In exemplary embodiments, the antigen binding protein is bispecific and binds to P2RY8 protein and a second antigen.

[0058] In exemplary instances, the second antigen is a cell surface protein expressed by a T-cell. In exemplary aspects, the cell surface protein is a component of the T-cell receptor (TCR), for example, CD3. In exemplary instances, the second antigen is a costimulatory molecule which assists in T-cell activation, e.g., CD40 or 4-1BB (CD137). In exemplary aspects, the second antigen is an Fc receptor. In various aspects, the Fc receptor is a Fc gamma receptor, Fc-alpha receptor, Fc-epsilon receptor. In exemplary aspects, the Fc receptor is CD64 (Fc-gamma RI), CD32 (Fc-gamma RIIA), CD16A (Fc-gamma RIIIA), CD16b (Fc-gamma RIIIb), FcεRI, CD23 (Fc-epsilon RII), CD89 (Fc-epsilon RI), Fcα/μR, or FcRn. In exemplary aspects, the Fc receptor is CD16A. In exemplary instances, the second antigen is an immune checkpoint molecule, e.g., a protein involved in the immune checkpoint pathway. The immune checkpoint pathway and molecules or proteins that function in it are known in the art. See, e.g., Pardoll, Nat Rev Genet 12(4): 252-264 (2012). In exemplary instances, the immune checkpoint molecule is A2AR, B7-H3, B7-H4, BTLA, CTLA4, IDO, KIR, LAG3, NOX2, PD-1, TIM3, VISTA, or SIGLEC7. Optionally, the immune checkpoint molecule is PD-1, LAG3, TIM3, or CTLA4.

[0059] Over fifty formats of bispecific antigen-binding proteins are known in the art, some of which are described in Kontermann and Brinkmann, Drug Discovery Today 20(7): 838-847 (2015); Brinkmann and Kontermann, mAbs 9(2): 182-212 (2017); Zhang et al., Exp Hematol Oncol 6:12 (2017); Spiess et al., Mol Immunol.; 67(2 Pt A):95-106 (2015); Front Immunol 12:626616 (2021). In exemplary aspects, the bispecific antigen-binding protein of the present disclosure is made through chemical engineering, genetic engineering, or quadroma technology.

[0060] In exemplary aspects, the bispecific antigen-binding protein is constructed with some or all of the constant domains of an antibody. In exemplary aspects, the bispecific antigen-binding protein of the present disclosure comprises an Fc polypeptide and retains Fc-mediated effector functions. In various instances, the bispecific antigen-binding protein is a bispecific monoclonal antibody formed by, e.g., chemical cross-linking of two monoclonal antibodies (mabs), or by "knobs-into-holes" technology. In exemplary aspects, the bispecific antigen-binding protein is made through "knobs-into-holes" technology in which H chain heterodimerization is forced by introducing different mutations into the two CH3 domains resulting in asymmetric antibodies. A "knob" mutation is made into one HC and a "hole" mutation is created in the other HC to promote heterodimerization. In exemplary aspects, the bispecific antigen-binding protein is a bispecific antibody produced by quadroma technology which is based on the somatic fusion of two different hybridoma cells producing monoclonal antibodies with the desired specificity (Zhang et al., 2017), supra. In exemplary aspects, the bispecific antigen-binding protein is a crossMab, ortho-Fab IgG, DVD-Ig, two in one IgG, IgG-scFv and $scFv_2$-Fc (Kontermann and Brinkmann, 2015), supra. In various aspects, the bispecific antigen-binding protein is an Ig-scFv fusion wherein a new antigen-binding moiety is added to a full-length IgG resulting in a fusion protein with tetravalency for two distinct antigens, e.g., IgG C-terminal scFv fusion and IgG N-terminal scFv fusion. In exemplary instances, the bispecific antigen-binding protein is a dual-variable-domain-IgG (DVD-IgG), wherein the LC and HC variable regions of an IgG specific for one antigen are fused to the N-terminal LC and HC variable regions of an IgG specific for a second antigen through a linker to form a DVD-IgG. In exemplary aspects, the bispecific antigen-binding protein is a diabody-Fc fusion which involves the replacement of a Fab fragment of an IgG with a bispecific diabody.

[0061] In alternative instances, the bispecific antigen-binding protein of the present disclosure does not comprise an Fc polypeptide. In exemplary aspects, the bispecific antigen-binding protein comprises the variable domains of each parental monoclonal antibody, and linkers are cloned and linked to form a single-chain bispecific antibody. In exemplary aspects, the bispecific antigen-binding protein is a tandem scFvs, diabody format, single-chain diabodies, tandem diabodies (TandAbs), dual-affinity retargeting molecules (DARTs), dock-and-lock (DNL), and nanobodies (Fan et al., J Hematol Oncol. 2015; 8:130). In various aspects, the bispecific antigen-binding protein is a bispecific $F(ab')_2$, an scFv, a bispecific diabody (BsDb), single-chain bispecific diabody (scBsDb),

single-chain bispecific tandem variable domain (scBsTaFv), dock-and-lock trivalent Fab (DNL-$(Fab)_3$), single-domain antibody (sdAb), or a bispecific single-domain antibody (BssdAb). In exemplary aspects, the bispecific antigen-binding protein is a tandem scFv comprising two scFv fragments linked by an extra peptide linker such as glycine-serine repeat motifs. Optionally, the tandem scFv comprises the structure: VL_A-linker1–VH_A-linker2–VH_B-linker3–VL_B (VL and VH derive from the single chain antibody fragment; A and B represent the parental monoclonal antibody A and B). In exemplary aspects, the bispecific antigen-binding protein is a TandAb which contains two pairs of VL and VH domains connected in a single polypeptide chain (Reusch et al., MAbs. 2015; 7(3):584-604). Two polypeptide products dimerize in a head-to-tail fashion, forming homodimers with large molecular weight (~105 kDa) upon expression. In exemplary aspects, the bispecific antigen-binding protein is one produced using crossMab technology which is described in PNAS 108(27): 11187-92 (2011). CrossMabs do not have any chemical linkers or connectors and are produced by a method that enforces correct light chain association in bispecific heterodimeric IgG antibodies. In exemplary aspects, the CrossMab is a bi- (1+1), tri- (2+1) and tetra-(2+2) valent bispecific crossMab, or is a non-Fc tandem antigen-binding fragment (Fab)-based crossMab. In exemplary instances, the crossMab is a $crossMab^{Fab}$, a $crossMab^{VH\text{-}VL}$, or a $crossMab^{CH1\text{-}CL}$.

[0062] In exemplary aspects, the bispecific antigen-binding protein comprises a single-domain antibody, or a nanobody, comprising a single monomeric variable antibody domain. Optionally, the variable domain is based on the heavy chain variable domain. In alternative aspects, the variable domain is based on the light chain variable domain.

[0063] In exemplary aspects, the bispecific antigen-binding protein is a bispecific T cell engager or BiTE®. BiTEs are bivalent small molecules comprising only the variable regions of antibodies in the form of scFvs which are connected by flexible peptidic linkers. In exemplary aspects, the bispecific antigen-binding protein comprises an scFv comprising the LC and HC variable regions of the presently disclosed P2RY8 antibodies and the LC and HC variable regions of a second antibody specific for a second antigen. In some embodiments, the BiTE comprises the LC and HC variable region of a second antibody specific for CD3. In some embodiments, the CD3 is CD3E.

[0064] In exemplary instances, the bispecific antigen-binding protein is a dual affinity retargeting (DART), which unlike BiTEs®, the covalent linkage between the two chains of DARTs limits the freedom of the antigen-binding sites. Therefore, DARTs are structurally

compact and can form stable contacts between target and effector cells. The DART comprises two engineered Fv fragments which have their own VH exchanged with the VH of the other one. The inter-exchanged Fv domains advantageously releases variant fragments from the conformational constraint by the short linking peptide.

[0065] In exemplary aspects, the bispecific antigen binding protein is an HSABody comprising two scFvs fused to modified HSA. HSABodies are described in McDonagh et al., Mol Cancer Ther. 2012;11(3):582–93.

[0066] Accordingly, in exemplary aspects, the bispecific antigen-binding protein comprises an antigen binding fragment of any of the presently disclosed P2RY8 antibodies. In exemplary aspects, the bispecific antigen-binding protein comprises a Fab of any of the presently disclosed P2RY8 antibodies. In exemplary aspects, the bispecific antigen-binding protein comprises a Fab of any of the presently disclosed P2RY8 antibodies and a Fab of a second antibody specific for a second antigen. In exemplary aspects, the bispecific antigen-binding protein comprises a $F(ab)_2$ of any of the presently disclosed P2RY8 antibodies. In exemplary aspects, the bispecific antigen-binding protein comprises a F(ab') of any of the presently disclosed P2RY8 antibodies. In exemplary aspects, the bispecific antigen-binding protein comprises a F(ab') of any of the presently disclosed P2RY8 antibodies and a F(ab') of a second antibody specific for a second antigen. In exemplary aspects, the bispecific antigen-binding protein comprises a $F(ab')_2$ of any of the presently disclosed P2RY8 antibodies In exemplary aspects, the bispecific antigen-binding protein comprises an scFv comprising the LC and HC variable regions of any of the presently disclosed P2RY8 antibodies. In various aspects, the antigen binding fragment is based on the heavy chain variable region and in other aspects, the antigen binding fragment is based on the light chain variable region. In exemplary aspects, the antigen binding fragment comprises at least part of both HC variable region and LC variable region. In exemplary aspects, the bispecific antigen-binding protein comprises at least one if not both of the LC or HC variable regions of the presently disclosed P2RY8 antibodies and at least one if not both of the LC and HC variable regions of a second antibody specific for a second antigen. In exemplary instances, the bispecific antigen-binding protein comprises a scFv comprising the LC and HC variable regions of the presently disclosed P2RY8 antibodies and the LC and HC variable regions of a second antibody specific for a second antigen.

[0067] *Nucleic acids*

[0068] The present disclosure further provides nucleic acids comprising a nucleotide

sequence encoding an antigen-binding protein of the present disclosure. By "nucleic acid" as used herein includes "polynucleotide," "oligonucleotide," and "nucleic acid molecule," and generally means a polymer of DNA or RNA, or modified forms thereof, which can be single-stranded or double-stranded, synthesized or obtained (e.g., isolated and/or purified) from natural sources, which can contain natural, non-natural or altered nucleotides, and which can contain a natural, non-natural or altered inter-nucleotide linkage, such as a phosphoroamidate linkage or a phosphorothioate linkage, instead of the phosphodiester found between the nucleotides of an unmodified oligonucleotide. The nucleic acid can comprise any nucleotide sequence which encodes any of the antigen-binding proteins of the present disclosure. Examples are shown in Tables 5 and 6, and SEQ ID NOS: 324-363.

[0069] The invention further provides nucleic acid molecules encoding the amino acid sequence corresponding to the antigen-binding proteins of the invention. In one embodiment, the nucleic acid molecule is a DNA (e.g., cDNA) or a hybrid thereof. Alternatively, the molecules is RNA or a hybrid thereof.

[0070] In some aspects, the nucleic acids of the present disclosure are recombinant. As used herein, the term "recombinant" refers to (i) molecules that are constructed outside living cells by joining natural or synthetic nucleic acid segments to nucleic acid molecules that can replicate in a living cell, or (ii) molecules that result from the replication of those described in (i) above. For purposes herein, the replication can be *in vitro* replication or *in vivo* replication.

[0071] The nucleic acids in some aspects are constructed based on chemical synthesis and/or enzymatic ligation reactions using procedures known in the art. See, for example, Sambrook et al. (1989) *Molecular Cloning: A Laboratory Manual*, 2nd ed, Plainview, N.Y.: Cold Spring Harbor Laboratory Press; and Ausubel et al. (1989) *Current Protocols in Molecular Biology,* New York: Greene Publishing and Wiley Interscience. For example, a nucleic acid can be chemically synthesized using naturally occurring nucleotides or variously modified nucleotides designed to increase the biological stability of the molecules or to increase the physical stability of the duplex formed upon hybridization (e.g., phosphorothioate derivatives and acridine substituted nucleotides). Examples of modified nucleotides that can be used to generate the nucleic acids include, but are not limited to, 5-fluorouracil, 5-bromouracil, 5-chlorouracil, 5-iodouracil, hypoxanthine, xanthine, 4-acetylcytosine, 5-(carboxyhydroxymethyl) uracil, 5- carboxymethylaminomethyl-2-thiouridine, 5-carboxymethylaminomethyluracil, dihydrouracil, beta-D-galactosylqueosine,

inosine, N^6-isopentenyladenine, 1-methylguanine, 1-methylinosine, 2,2-dimethylguanine, 2-methyladenine, 2-methylguanine, 3-methylcytosine, 5-methylcytosine, N-substituted adenine, 7-methylguanine, 5-methylaminomethyluracil, 5- methoxyaminomethyl-2-thiouracil, beta-D-mannosylqueosine, 5'- methoxycarboxymethyluracil, 5-methoxyuracil, 2-methylthio-N^6-isopentenyladenine, uracil-5-oxyacetic acid (v), wybutoxosine, pseudouracil, queosine, 2-thiocytosine, 5-methyl-2- thiouracil, 2-thiouracil, 4-thiouracil, 5-methyluracil, uracil-5-oxyacetic acid methylester, 3-(3-amino-3-N-2-carboxypropyl)uracil, and 2,6-diaminopurine. Alternatively, one or more of the nucleic acids of the present disclosure can be purchased from companies, such as Macromolecular Resources (Fort Collins, CO) and Synthegen (Houston, TX).

[0072] *Vector*

[0073] The nucleic acids of the present disclosure in some aspects are incorporated into a vector. In this regard, the present disclosure provides vectors comprising any of the presently disclosed nucleic acids. In various aspects, the vector is a recombinant expression vector. For purposes herein, the term "recombinant expression vector" means a genetically modified oligonucleotide or polynucleotide construct that permits the expression of a mRNA, protein, polypeptide, or peptide by a host cell, when the construct comprises a nucleotide sequence encoding the mRNA, protein, polypeptide, or peptide, and the vector is contacted with the cell under conditions sufficient to have the mRNA, protein, polypeptide, or peptide expressed within the cell. The vectors of the present disclosure are not naturally occurring as a whole. However, parts of the vectors can be naturally occurring. The presently disclosed vectors can comprise any type of nucleotides, including, but not limited to DNA and RNA, which can be single-stranded or double-stranded, synthesized or obtained in part from natural sources, and which can contain natural, non-natural or altered nucleotides. The vectors can comprise naturally occurring or non-naturally occurring internucleotide linkages, or both types of linkages. In some aspects, the altered nucleotides or non-naturally occurring internucleotide linkages do not hinder the transcription or replication of the vector.

[0074] The vector of the present disclosure can be any suitable vector, and can be used to transduce, transform or transfect any suitable host. Suitable vectors include those designed for propagation and expansion or for expression or both, such as plasmids and viruses. The vector can be a plasmid-based expression vector. In various aspects, the vector is selected from the group consisting of the pUC series (Fermentas Life Sciences), the pBluescript

series (Stratagene, La Jolla, CA), the pET series (Novagen, Madison, WI), the pGEX series (Pharmacia Biotech, Uppsala, Sweden), and the pEX series (Clontech, Palo Alto, CA). Bacteriophage vectors, such as λGTIO, λGTl 1, λZapII (Stratagene), λEMBL4, and λNMl 149, also can be used. Examples of plant expression vectors include pBIOl, pBI101.2, pBI101.3, pBI121 and pBIN19 (Clontech). Examples of animal expression vectors include pEUK-Cl, pMAM and pMAMneo (Clontech). In some aspects, the vector is a viral vector, e.g., a retroviral vector. In various aspects, the vector is an adenovirus vector, an adeno-associated virus (AAV) vector, a herpes simplex virus (HSV) vector, a vesicular stomatitis virus (VSV) vector, vaccinia virus vector, or lentivirus vector. See, e.g., Howarth et al., Cell Biol. Toxicol. 26(1): 1-20 (2010). In various aspects, the vector is a baculovirus vector which infects arthropods, e.g., insects. In various aspects, the baculovirus vector is an Autographa californica multiple nuclear virus (AcMNPV) or a Bombyx mori nuclear polyhedrosis virus (BmNPV). See, e.g., Khan, Adv Pharm Bull 3(2): 257-263 (2013); Miller, Bioessays 11(4): 91-96 (1989); Atkinson et al., Pestic Sci 28: 215-224 (1990).

[0075] Table 1 below provides a list of anti-P2YR8 antibody names along with synonymous names, and corresponding expression vector names with notable features of the anti-P2YR8 antibodies.

Table 1: Names of exemplary anti-P2YR8 antibodies and their expression vectors

Antibody name	**Antibody expression vector name**	**Note**
P2RY8 mAb-690 (also referred to herein as 10-0690-m)	p10-0690-m	Chimeric anti-P2RY8 antibody: Isolate 690 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region
P2RY8 mAb-695 (also referred to herein as 10-0695-m)	p10-0695-m	Chimeric anti-P2RY8 antibody: Isolate 695 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region

P2RY8 mAb-701 (also referred to herein as 10-0701-m)	p10-0701-m	Chimeric anti-P2RY8 antibody: Isolate 701 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region
P2RY8 mAb-716 (also referred to herein as P2RY8mAb-716, 10-0716-m, 716-m, 716-m (hIgG1), 0716m or 716)	p10-0716-m	Chimeric anti-P2RY8 antibody: Isolate 716 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region
P2RY8 mAb-720 (also referred to herein as 10-0720-m)	p10-0720-m	Chimeric anti-P2RY8 antibody: Isolate 720 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region
P2RY8 mAb-724 (also referred to herein as 10-0724-m)	p10-0724-m	Chimeric anti-P2RY8 antibody: Isolate 724 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region
P2RY8 mAb-725 (also referred to herein as 10-0725-m)	p10-0725-m	Chimeric anti-P2RY8 antibody: Isolate 725 mouse anti-P2RY8 mAb constant region replaced with human IgG1-λ constant region
P2RY8 mAb-728 (also referred to herein as 10-0728-m)	p10-0728-m	Chimeric anti-P2RY8 antibody: Isolate 728 mouse anti-P2RY8 mAb constant region replaced with human IgG1-κ constant region
P2RY8 mAb-729 (also referred to herein as 10-0729-m)	p10-0729-m	Chimeric anti-P2RY8 antibody: Isolate 729 mouse anti-P2RY8 mAb constant

		region replaced with human IgG1-κ constant region
P2RY8 mAb-716-h1 (also referred to herein as P2RY8mAb-716-h1, P2RY8hAb 0716-h1, 10-0716-h1, or 716-h1)	p10-0716-h1	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8 antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 1
P2RY8 mAb-716-h2 (also referred to herein as P2RY8mAb-716-h2, P2RY8hAb 0716-h2, 10-0716-h2, or 716-h2)	p10-0716-h2	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8 antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 2
P2RY8 mAb-716-h3 (also referred to herein as P2RY8mAb-716-h3, P2RY8hAb 0716-h3, 10-0716-h3, or 716-h3)	p10-0716-h3	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8 antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 3
P2RY8 mAb-716-h4 (also referred to herein as P2RY8mAb-716-h4, P2RY8hAb 0716-h4, 10-0716-h4, or 716-h4)	p10-0716-h4	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8 antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 4
P2RY8 mAb-716-h5 (also referred to herein as P2RY8mAb-716-h5,	p10-0716-h5	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8

P2RY8hAb 0716-h5, 10-0716-h5, or 716-h5)		antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 5
P2RY8 mAb-716-h6 (also referred to herein as P2RY8mAb-716-h6, P2RY8hAb 0716-h6, 10-0716-h6, or 716-h6)	p10-0716-h6	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8 antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 6
P2RY8 mAb-716-h8 (also referred to herein as P2RY8mAb-716-h8, P2RY8hAb 0716-h8, 10-0716-h8, or 716-h8)	p10-0716-h8	Humanized anti-P2RY8 antibody comprising CDRs of 10-0716-m anti-P2RY8 antibody and/or its CDR variants and framework and constant regions of human IgG1-κ antibody, version 8
P2RY8 mAb-724-h3 (also referred to herein as P2RY8mAb-724-h3, P2RY8hAb 0724-h3, 10-0724-h3, or 724-h3)	p10-0724-h3	Humanized anti-P2RY8 antibody comprising CDRs of 10-0724-m anti-P2RY8 antibody and framework and constant regions of human IgG1-κ antibody, version 3
P2RY8 mAb-724-h4 (also referred to herein as P2RY8mAb-724-h4, P2RY8hAb 0724-h4, 10-0724-h4, or 724-h4)	p10-0724-h4	Humanized anti-P2RY8 antibody comprising CDRs of 10-0724-m anti-P2RY8 antibody and framework and constant regions of human IgG1-κ antibody, version 4
P2RY8 mAb-724-h5 (also referred to herein as P2RY8mAb-724-h5,	p10-0724-h5	Humanized anti-P2RY8 antibody comprising CDRs of 10-0724-m anti-P2RY8

P2RY8hAb 0724-h5, 10-0724-h5, or 724-h5)		antibody and framework and constant regions of human IgG1-κ antibody, version 5
P2RY8 mAb-724-h6 (also referred to herein as P2RY8mAb-724-h6, P2RY8hAb 0724-h6, 10-0724-h6, or 724-h6)	p10-0724-h6	Humanized anti-P2RY8 antibody comprising CDRs of 10-0724-m anti-P2RY8 antibody and framework and constant regions of human IgG1-κ antibody, version 6

[0076] The vectors of the present disclosure can be prepared using standard recombinant DNA techniques described in, for example, Sambrook et al., supra, and Ausubel et al., supra. Constructs of expression vectors, which are circular or linear, can be prepared to contain a replication system functional in a prokaryotic or eukaryotic host cell. Replication systems can be derived, e.g., from ColE1, 2μ plasmid, λ, SV40, bovine papilloma virus, and the like.

[0077] In some aspects, the vector comprises regulatory sequences, such as transcription and translation initiation and termination codons, which are specific to the type of host (e.g., bacterium, fungus, plant, or animal) into which the vector is to be introduced, as appropriate and taking into consideration whether the vector is DNA- or RNA-based.

[0078] The vector can include one or more marker genes, which allow for selection of transformed or transfected hosts. Marker genes include biocide resistance, e.g., resistance to antibiotics, heavy metals, etc., complementation in an auxotrophic host to provide prototrophy, and the like. Suitable marker genes for the presently disclosed expression vectors include, for instance, neomycin/G418 resistance genes, hygromycin resistance genes, histidinol resistance genes, tetracycline resistance genes, and ampicillin resistance genes.

[0079] The vector can comprise a native or normative promoter operably linked to the nucleotide sequence encoding the polypeptide (including functional portions and functional variants thereof), or to the nucleotide sequence which is complementary to or which hybridizes to the nucleotide sequence encoding the polypeptide. The selection of promoters, e.g., strong, weak, inducible, tissue-specific and developmental-specific, is within the ordinary skill of the artisan. Similarly, the combining of a nucleotide sequence with a

promoter is also within the skill of the artisan. The promoter can be a non-viral promoter or a viral promoter, e.g., a cytomegalovirus (CMV) promoter, an SV40 promoter, an RSV promoter, and a promoter found in the long-terminal repeat of the murine stem cell virus.

[0080] *Host cells*

[0081] Provided herein are host cells comprising a nucleic acid or vector of the present disclosure. As used herein, the term "host cell" refers to any type of cell that can contain the presently disclosed vector and is capable of producing an expression product encoded by the nucleic acid (e.g., mRNA, protein). The host cell in some aspects is an adherent cell or a suspended cell, i.e., a cell that grows in suspension. The host cell in various aspects is a cultured cell or a primary cell, i.e., isolated directly from an organism, e.g., a human. The host cell can be of any cell type, can originate from any type of tissue, and can be of any developmental stage.

[0082] In various aspects, the antigen-binding protein is a glycosylated protein and the host cell is a glycosylation-competent cell. In various aspects, the glycosylation-competent cell is an eukaryotic cell, including, but not limited to, a yeast cell, filamentous fungi cell, protozoa cell, algae cell, insect cell, or mammalian cell. Such host cells are described in the art. See, e.g., Frenzel, et al., *Front Immunol* 4: 217 (2013). In various aspects, the eukaryotic cells are mammalian cells. In various aspects, the mammalian cells are non-human mammalian cells. In some aspects, the cells are Chinese Hamster Ovary (CHO) cells and derivatives thereof (e.g., CHO-K1, CHO pro-3), mouse myeloma cells (e.g., NS0, GS-NS0, Sp2/0), cells engineered to be deficient in dihydrofolatereductase (DHFR) activity (e.g., DUKX-X11, DG44), human embryonic kidney 293 (HEK293) cells or derivatives thereof (e.g., HEK293T, HEK293-EBNA), green African monkey kidney cells (e.g., COS cells, VERO cells), human cervical cancer cells (e.g., HeLa), human bone osteosarcoma epithelial cells U2-OS, adenocarcinomic human alveolar basal epithelial cells A549, human fibrosarcoma cells HT1080, mouse brain tumor cells CAD, embryonic carcinoma cells P19, mouse embryo fibroblast cells NIH 3T3, mouse fibroblast cells L929, mouse neuroblastoma cells N2a, human breast cancer cells MCF-7, retinoblastoma cells Y79, human retinoblastoma cells SO-Rb50, human liver cancer cells Hep G2, mouse B myeloma cells J558L, or baby hamster kidney (BHK) cells (Gaillet et al. 2007; Khan, Adv Pharm Bull 3(2): 257-263 (2013)).

[0083] For purposes of amplifying or replicating the vector, the host cell is in some aspects is a prokaryotic cell, e.g., a bacterial cell.

[0084] Also provided by the present disclosure is a population of cells comprising at least one host cell described herein. The population of cells in some aspects is a heterogeneous population comprising the host cell comprising vectors described, in addition to at least one other cell, which does not comprise any of the vectors. Alternatively, in some aspects, the population of cells is a substantially homogeneous population, in which the population comprises mainly host cells (e.g., consisting essentially of) comprising the vector. The population in some aspects is a clonal population of cells, in which all cells of the population are clones of a single host cell comprising a vector, such that all cells of the population comprise the vector. In various embodiments of the present disclosure, the population of cells is a clonal population comprising host cells comprising a vector as described herein.

[0085] *Manufacture methods*

[0086] Also provided herein are methods of producing an antigen-binding protein which binds to P2RY8 protein. In various embodiments, the method comprises culturing a host cell comprising a nucleic acid comprising a nucleotide sequence encoding the antigen-binding protein as described herein in a cell culture medium and harvesting the antigen-binding protein from the cell culture medium. The host cell can be any of the host cells described herein. In various aspects, the host cell is selected from the group consisting of: CHO cells, NS0 cells, COS cells, VERO cells, and BHK cells. In various aspects, the step of culturing a host cell comprises culturing the host cell in a growth medium to support the growth and expansion of the host cell. In various aspects, the growth medium increases cell density, culture viability and productivity in a timely manner. In various aspects, the growth medium comprises amino acids, vitamins, inorganic salts, glucose, and serum as a source of growth factors, hormones, and attachment factors. In various aspects, the growth medium is a fully chemically defined media consisting of amino acids, vitamins, trace elements, inorganic salts, lipids and insulin or insulin-like growth factors. In addition to nutrients, the growth medium also helps maintain pH and osmolality. Several growth media are commercially available and are described in the art. See, e.g., Arora, "Cell Culture Media: A Review" MATER METHODS 3:175 (2013).

[0087] In various aspects, the method comprises culturing the host cell in a feed medium. In various aspects, the method comprises culturing in a feed medium in a fed-batch mode. Methods of recombinant protein production are known in the art. See, e.g., Li et al., "Cell culture processes for monoclonal antibody production" MAbs 2(5): 466–477 (2010).

[0088] The method of making an antigen-binding protein can comprise one or more steps for purifying the protein from a cell culture or the supernatant thereof and preferably recovering the purified protein. In various aspects, the method comprises one or more chromatography steps, e.g., affinity chromatography (e.g., protein A affinity chromatography), ion exchange chromatography, hydrophobic interaction chromatography. In various aspects, the method comprises purifying the protein using a Protein A affinity chromatography resin.

[0089] In various embodiments, the method further comprises steps for formulating the purified protein, etc., thereby obtaining a formulation comprising the purified protein. Such steps are described in Formulation and Process Development Strategies for Manufacturing, eds. Jameel and Hershenson, John Wiley & Sons, Inc. (Hoboken, NJ), 2010.

[0090] In various aspects, the antigen-binding protein is linked to a polypeptide and the antigen-binding protein is part of a fusion protein. Thus, the present disclosure further provides methods of producing a fusion protein comprising an antigen-binding protein which binds to P2RY8 protein. In various embodiments, the method comprises culturing a host cell comprising a nucleic acid comprising a nucleotide sequence encoding the fusion protein as described herein in a cell culture medium and harvesting the fusion protein from the cell culture medium.

[0091] *Conjugates*

[0092] The present disclosure also provides antigen-binding proteins attached, linked or conjugated to a second moiety (e.g., a heterologous moiety, a conjugate moiety). Accordingly, the present disclosure provides a conjugate comprising an antigen-binding protein and a heterologous moiety. As used herein, the term “heterologous moiety” is synonymous with “conjugate moiety” and refers to any molecule (chemical or biochemical, naturally occurring or non-coded) which is different from the antigen-binding proteins of the present disclosure. Various heterologous moieties include, but are not limited to, a polymer, a carbohydrate, a lipid, a nucleic acid, an oligonucleotide, a DNA or RNA, an amino acid, peptide, polypeptide, protein, therapeutic agent (e.g., a cytotoxic agent, cytokine), or a diagnostic agent.

[0093] In some embodiments, the heterologous moiety is a polymer. The polymer can be branched or unbranched. The polymer can be of any molecular weight. The polymer in some embodiments has an average molecular weight of between about 2 kDa to about 100 kDa (the term "about" indicating that in preparations of a water-soluble polymer, some

molecules will weigh more, some less, than the stated molecular weight). The average molecular weight of the polymer is in some aspect between about 5 kDa and about 50 kDa, between about 12 kDa to about 40 kDa or between about 20 kDa to about 35 kDa.

[0094] In some embodiments, the polymer is modified to have a single reactive group, such as an active ester for acylation or an aldehyde for alkylation, so that the degree of polymerization can be controlled. The polymer in some embodiments is water soluble so that the protein to which it is attached does not precipitate in an aqueous environment, such as a physiological environment. In some embodiments, when, for example, the composition is used for therapeutic use, the polymer is pharmaceutically acceptable. Additionally, in some aspects, the polymer is a mixture of polymers, e.g., a co-polymer, a block co-polymer.

[0095] In some embodiments, the polymer is selected from the group consisting of: polyamides, polycarbonates, polyalkylenes and derivatives thereof including, polyalkylene glycols, polyalkylene oxides, polyalkylene terephthalates, polymers of acrylic and methacrylic esters, including poly(methyl methacrylate), poly(ethyl methacrylate), poly(butyl methacrylate), poly(isobutyl methacrylate), poly(hexyl methacrylate), poly(isodecyl methacrylate), poly(lauryl methacrylate), poly(phenyl methacrylate), poly(methyl acrylate), poly(isopropyl acrylate), poly(isobutyl acrylate), and poly(octadecyl acrylate), polyvinyl polymers including polyvinyl alcohols, polyvinyl ethers, polyvinyl esters, polyvinyl halides, poly(vinyl acetate), and polyvinylpyrrolidone, polyglycolides, polysiloxanes, polyurethanes and co-polymers thereof, celluloses including alkyl cellulose, hydroxyalkyl celluloses, cellulose ethers, cellulose esters, nitro celluloses, methyl cellulose, ethyl cellulose, hydroxypropyl cellulose, hydroxy-propyl methyl cellulose, hydroxybutyl methyl cellulose, cellulose acetate, cellulose propionate, cellulose acetate butyrate, cellulose acetate phthalate, carboxyethyl cellulose, cellulose triacetate, and cellulose sulphate sodium salt, polypropylene, polyethylenes including poly(ethylene glycol), poly(ethylene oxide), and poly(ethylene terephthalate), and polystyrene.

[0096] A particularly preferred water-soluble polymer for use herein is polyethylene glycol (PEG). As used herein, polyethylene glycol is meant to encompass any of the forms of PEG that can be used to derivatize other proteins, such as mono-(C1-C10) alkoxy- or aryloxy-polyethylene glycol. PEG is a linear or branched neutral polyether, available in a broad range of molecular weights, and is soluble in water and most organic solvents.

[0097] In some embodiments, the heterologous moiety is a carbohydrate. In some embodiments, the carbohydrate is a monosaccharide (e.g., glucose, galactose, fructose), a disaccharide (e.g., sucrose, lactose, maltose), an oligosaccharide (e.g., raffinose, stachyose), or a polysaccharide (a starch, amylase, amylopectin, cellulose, chitin, callose, laminarin, xylan, mannan, fucoidan, galactomannan).

[0098] In some embodiments, the heterologous moiety is a lipid. The lipid, in some embodiments, is a fatty acid, eicosanoid, prostaglandin, leukotriene, thromboxane, N-acyl ethanolamine), glycerolipid (e.g., mono-, di-, tri-substituted glycerols), glycerophospholipid (e.g., phosphatidylcholine, phosphatidylinositol, phosphatidylethanolamine, phosphatidylserine), sphingolipid (e.g., sphingosine, ceramide), sterol lipid (e.g., steroid, cholesterol), prenol lipid, saccharolipid, a polyketide, oil, wax, cholesterol, sterol, fat-soluble vitamin, monoglyceride, diglyceride, triglyceride, or a phospholipid.

[0099] In some embodiments, the heterologous moiety is a therapeutic agent. The therapeutic agent can be any of those known in the art. Examples of therapeutic agents that are contemplated herein include, but are not limited to, natural enzymes, proteins derived from natural sources, recombinant proteins, natural peptides, synthetic peptides, cyclic peptides, antibodies, receptor agonists, cytotoxic agents, immunoglobins, beta-adrenergic blocking agents, calcium channel blockers, coronary vasodilators, cardiac glycosides, antiarrhythmics, cardiac sympathomimetics, angiotensin converting enzyme (ACE) inhibitors, diuretics, inotropes, cholesterol and triglyceride reducers, bile acid sequestrants, fibrates, 3-hydroxy-3-methylgluteryl (HMG)-CoA reductase inhibitors, niacin derivatives, antiadrenergic agents, alpha-adrenergic blocking agents, centrally acting antiadrenergic agents, vasodilators, potassium-sparing agents, thiazides and related agents, angiotensin II receptor antagonists, peripheral vasodilators, antiandrogens, estrogens, antibiotics, retinoids, insulins and analogs, alpha-glucosidase inhibitors, biguanides, meglitinides, sulfonylureas, thiazolidinediones, androgens, progestogens, bone metabolism regulators, anterior pituitary hormones, hypothalamic hormones, posterior pituitary hormones, gonadotropins, gonadotropin-releasing hormone antagonists, ovulation stimulants, selective estrogen receptor modulators, antithyroid agents, thyroid hormones, bulk forming agents, laxatives, antiperistalsis, flora modifiers, intestinal adsorbents, intestinal anti-infectives, antianorexic, anti-cachexic, anti-bulimics, appetite suppressants, anti-obesity agents, antacids, upper gastrointestinal tract agents, anticholinergic agents, aminosalicylic acid derivatives, biological response modifiers, corticosteroids, antispasmodics, 5-HT_4 partial

agonists, antihistamines, cannabinoids, dopamine antagonists, serotonin antagonists, cytoprotectives, histamine H2-receptor antagonists, mucosal protective agent, proton pump inhibitors, H. pylori eradication therapy, erythropoiesis stimulants, hematopoietic agents, anemia agents, heparins, antifibrinolytics, hemostatics, blood coagulation factors, adenosine diphosphate inhibitors, glycoprotein receptor inhibitors, fibrinogen-platelet binding inhibitors, thromboxane-A_2 inhibitors, plasminogen activators, antithrombotic agents, glucocorticoids, mineralocorticoids, corticosteroids, selective immunosuppressive agents, antifungals, drugs involved in prophylactic therapy, drugs used to treat AIDS-associated infections, cytomegalovirus, non-nucleoside reverse transcriptase inhibitors, nucleoside analog reverse transcriptase inhibitors, protease inhibitors, drugs used to treat or prevent anemia, drugs used to treat Kaposi's sarcoma, aminoglycosides, carbapenems, cephalosporins, glycopeptides, lincosamides, macrolides, oxazolidinones, penicillins, streptogramins, sulfonamides, trimethoprim and derivatives, tetracyclines, anthelmintics, amebicides, biguanides, cinchona alkaloids, folic acid antagonists, quinoline derivatives, drugs used in Pneumocystis carinii therapy, hydrazides, imidazoles, triazoles, nitroimidazoles, cyclic amines, neuraminidase inhibitors, nucleosides, phosphate binders, cholinesterase inhibitors, agents used in adjunctive therapy, barbiturates and derivatives, benzodiazepines, gamma aminobutyric acid derivatives, hydantoin derivatives, iminostilbene derivatives, succinimide derivatives, anticonvulsants, ergot alkaloids, anti-migraine preparations, biological response modifiers, carbamic acid eaters, tricyclic derivatives, depolarizing agents, nondepolarizing agents, neuromuscular paralytic agents, CNS stimulants, dopaminergic reagents, monoamine oxidase inhibitors, COMT inhibitors, alkyl sulphonates, ethylenimines, imidazotetrazines, nitrogen mustard analogs, nitrosoureas, platinum-containing compounds, antimetabolites, purine analogs, pyrimidine analogs, urea derivatives, anthracyclines, actinomycins, camptothecin derivatives, epipodophyllotoxins, taxanes, vinca alkaloids and analogs, antiandrogens, antiestrogens, nonsteroidal aromatase inhibitors, protein kinase inhibitor antineoplastics, azaspirodecanedione derivatives, anxiolytics, stimulants, monoamine reuptake inhibitors, selective serotonin reuptake inhibitors, antidepressants, benzisoxazole derivatives, butyrophenone derivatives, dibenzodiazepine derivatives, dibenzothiazepine derivatives, diphenylbutylpiperidine derivatives, phenothiazines, thienobenzodiazepine derivatives, thioxanthene derivatives, allergenic extracts, nonsteroidal agents, leukotriene receptor antagonists, xanthines, endothelin receptor antagonist, prostaglandins, lung surfactants, mucolytics, antimitotics,

uricosurics, xanthine oxidase inhibitors, phosphodiesterase inhibitors, methenamine salts, nitrofuran derivatives, quinolones, smooth muscle relaxants, parasympathomimetic agents, halogenated hydrocarbons, esters of amino benzoic acid, amides (e.g. lidocaine, articaine hydrochloride, bupivacaine hydrochloride), antipyretics, hypnotics and sedatives, cyclopyrrolones, pyrazolopyrimidines, nonsteroidal anti-inflammatory drugs, opioids, para-aminophenol derivatives, alcohol dehydrogenase inhibitor, heparin antagonists, adsorbents, emetics, opioid antagonists, cholinesterase reactivators, nicotine replacement therapy, vitamin A analogs and antagonists, vitamin B analogs and antagonists, vitamin C analogs and antagonists, vitamin D analogs and antagonists, vitamin E analogs and antagonists, and vitamin K analogs and antagonists.

[00100] The antigen-binding proteins of the present disclosure can be conjugated to one or more cytokines and growth factors that are effective in inhibiting tumor metastasis, and wherein the cytokine or growth factor has been shown to have an antiproliferative effect on at least one cell population. Such cytokines, lymphokines, growth factors, or other hematopoietic factors include, but are not limited to: M-CSF, GM-CSF, TNF, IL-1, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-9, IL-10, IL-11, IL-12, IL-13, IL-14, IL-15, IL-16, IL-17, IL-18, IFN, TNFα, TNF1, TNF2, G-CSF, Meg-CSF, GM-CSF, thrombopoietin, stem cell factor, and erythropoietin. Additional growth factors for use herein include angiogenin, bone morphogenic protein-1, bone morphogenic protein-2, bone morphogenic protein-3, bone morphogenic protein-4, bone morphogenic protein-5, bone morphogenic protein-6, bone morphogenic protein-7, bone morphogenic protein-8, bone morphogenic protein-9, bone morphogenic protein-10, bone morphogenic protein-11, bone morphogenic protein-12, bone morphogenic protein-13, bone morphogenic protein-14, bone morphogenic protein-15, bone morphogenic protein receptor IA, bone morphogenic protein receptor IB, brain derived neurotrophic factor, ciliary neurotrophic factor, ciliary neurotrophic factor receptor α, cytokine-induced neutrophil chemotactic factor 1, cytokine-induced neutrophil, chemotactic factor 2 α, cytokine-induced neutrophil chemotactic factor 2 β, β endothelial cell growth factor, endothelin 1, epithelial-derived neutrophil attractant, glial cell line-derived neurotrophic factor receptor α 1, glial cell line-derived neurotrophic factor receptor α 2, growth related protein, growth related protein α, growth related protein β, growth related protein γ, heparin binding epidermal growth factor, hepatocyte growth factor, hepatocyte growth factor receptor, insulin-like growth factor I, insulin-like growth factor receptor, insulin-like growth factor II, insulin-like growth factor binding protein,

keratinocyte growth factor, leukemia inhibitory factor, leukemia inhibitory factor receptor α, nerve growth factor nerve growth factor receptor, neurotrophin-3, neurotrophin-4, pre-B cell growth stimulating factor, stem cell factor, stem cell factor receptor, transforming growth factor α, transforming growth factor β, transforming growth factor β1, transforming growth factor β1.2, transforming growth factor β2, transforming growth factor β3, transforming growth factor β5, latent transforming growth factor β1, transforming growth factor β binding protein I, transforming growth factor β binding protein II, transforming growth factor β binding protein III, tumor necrosis factor receptor type I, tumor necrosis factor receptor type II, urokinase-type plasminogen activator receptor, and chimeric proteins and biologically or immunologically active fragments thereof.

[00101] In some embodiments, the conjugate comprises an antigen-binding protein as described herein and a cytotoxic agent. The cytotoxic agent is any molecule (chemical or biochemical) which is toxic to a cell. In some aspects, when a cytotoxic agent is conjugated to an antigen-binding protein of the present disclosure, the results obtained are synergistic. That is to say, the effectiveness of the combination therapy of an antigen-binding protein and the cytotoxic agent is synergistic, i.e., the effectiveness is greater than the effectiveness expected from the additive individual effects of each. Therefore, the dosage of the cytotoxic agent can be reduced and thus, the risk of the toxicity problems and other side effects is concomitantly reduced. In some embodiments, the cytotoxic agent is a chemotherapeutic agent. Chemotherapeutic agents are known in the art and include, but not limited to, platinum coordination compounds, topoisomerase inhibitors, antibiotics, antimitotic alkaloids and difluoronucleosides, as described in U.S. Pat. No. 6,630,124.

[00102] In some embodiments, the chemotherapeutic agent is a platinum coordination compound. The term "platinum coordination compound" refers to any tumor cell growth inhibiting platinum coordination compound that provides the platinum in the form of an ion.

[00103] In some embodiments, the platinum coordination compound is cis-diamminediaqua platinum(II) ion; chloro(diethylenetriamine)-platinum(II) chloride; dichloro(ethylenediamine)-platinum(II), diammine(1,1-cyclobutanedicarboxylato) platinum(II) (carboplatin); spiroplatin; iproplatin; diammine(2-ethylmalonato)-platinum(II); ethylenediamine platinum(II) malonate; aqua(1,2-diaminocyclohexane)-sulfatoplatinum(II); (1,2-diaminocyclohexane)malonatoplatinum(II); (4-caroxyphthalato)(1,2-diaminocyclohexane)platinum(II); (1,2-diaminocyclohexane)-(isocitrato)platinum(II); (1,2-

diaminocyclohexane)cis(pyruvato)platinum(II); (1,2-diaminocyclohexane)oxalatoplatinum(II); ormaplatin; and tetraplatin.

[00104] In some embodiments, cisplatin is the platinum coordination compound employed in the compositions and methods of the present invention. Cisplatin is commercially available under the name PLATINOL™ from Bristol Myers-Squibb Corporation and is available as a powder for constitution with water, sterile saline or other suitable vehicle. Other platinum coordination compounds suitable for use in the present invention are known and are available commercially and/or can be prepared by conventional techniques. Cisplatin, or cis-dichlorodiammineplatinum(II), has been used successfully for many years as a chemotherapeutic agent in the treatment of various human solid malignant tumors. More recently, other diamino-platinum complexes have also shown efficacy as chemotherapeutic agents in the treatment of various human solid malignant tumors. Such diamino-platinum complexes include, but are not limited to, spiroplatinum and carboplatinum. Although cisplatin and other diamino-platinum complexes have been widely used as chemotherapeutic agents in humans, they have had to be delivered at high dosage levels that can lead to toxicity problems, such as kidney damage.

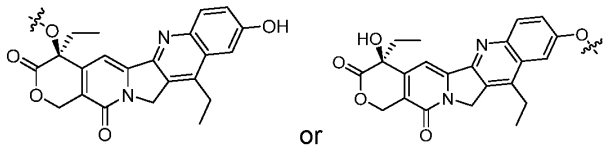
[00105] In some embodiments, the chemotherapeutic agent is a topoisomerase inhibitor. Topoisomerases are enzymes that are capable of altering DNA topology in eukaryotic cells. They are critical for cellular functions and cell proliferation. Generally, there are two classes of topoisomerases in eukaryotic cells, type I and type II. Topoisomerase I is a monomeric enzyme of approximately 100,000 molecular weight. The enzyme binds to DNA and introduces a transient single-strand break, unwinds the double helix (or allows it to unwind), and subsequently reseals the break before dissociating from the DNA strand. Various topoisomerase inhibitors have recently shown clinical efficacy in the treatment of humans afflicted with ovarian, cancer, esophageal cancer or non-small cell lung carcinoma.

[00106] In some aspects, the topoisomerase inhibitor is camptothecin or a camptothecin analog. Camptothecin is a water-insoluble, cytotoxic alkaloid produced by Camptotheca acuminata trees indigenous to China and Nothapodytes foetida trees indigenous to India. Camptothecin exhibits tumor cell growth inhibiting activity against a number of tumor cells. Compounds of the camptothecin analog class are typically specific inhibitors of DNA topoisomerase I. By the term "inhibitor of topoisomerase" is meant any tumor cell growth inhibiting compound that is structurally related to camptothecin. Compounds of the

camptothecin analog class include, but are not limited to; topotecan, irinotecan and 9-aminocamptothecin.

[00107] In additional embodiments, the cytotoxic agent is any tumor cell growth inhibiting camptothecin analog claimed or described in: U.S. Pat. No. 5,004,758, issued on Apr. 2, 1991 and European Patent Application Number 88311366.4, published on Jun. 21, 1989 as 20' Publication Number EP 0 321 122; U.S. Pat. No. 4,604,463, issued on Aug. 5, 1986 and European Patent Application Publication Number EP 0 137 145, published on Apr. 17, 1985; U.S. Pat. No. 4,473,692, issued on Sep. 25, 1984 and European Patent Application Publication Number EP 0 074 256, published on Mar. 16, 1983; U.S. Pat. No. 4,545,880, issued on Oct. 8, 1985 and European Patent Application Publication Number EP 0 074 256, published on Mar. 16, 1983; European Patent Application Publication Number EP 0 088 642, published on Sep. 14, 1983; Wani et al., J. Med. Chem., 29, 2358-2363 (1986); Nitta et al., Proc. 14th International Congr. Chemotherapy, Kyoto, 1985, Tokyo Press, Anticancer Section 1, p. 28-30, especially a compound referred to as CPT-11. CPT-11 is a camptothecin analog with a 4-(piperidino)-piperidine side chain joined through a carbamate linkage at C-10 of 10-hydroxy-7-ethyl camptothecin. CPT-11 is currently undergoing human clinical trials and is also referred to as irinotecan; Wani et al, J. Med. Chem., 23, 554 (1980); Wani et. al., J. Med. Chem., 30, 1774 (1987); U.S. Pat. No. 4,342,776, issued on Aug. 3, 1982; U.S. patent application Ser. No. 581,916, filed on Sep. 13, 1990 and European Patent Application Publication Number EP 418 099, published on Mar. 20, 1991; U.S. Pat. No. 4,513,138, issued on Apr. 23, 1985 and European Patent Application Publication Number EP 0 074 770, published on Mar. 23, 1983; U.S. Pat. No. 4,399,276, issued on Aug. 16, 1983 and European Patent Application Publication Number 0 056 692, published on Jul. 28, 1982; the entire disclosure of each of which is hereby incorporated by reference. All of the above-listed compounds of the camptothecin analog class are available commercially and/or can be prepared by conventional techniques including those described in the above-listed references. The topoisomerase inhibitor may be selected from the group consisting of topotecan, irinotecan and 9-aminocamptothecin.

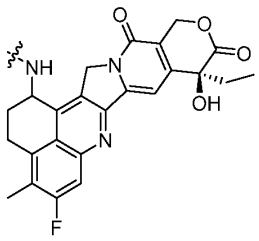
[00108] In some embodiments, the camptothecin analog is an active metabolite of irinotecan (CPT-11). In some such embodiments, the camptothecin analog is 7-ethyl-10-hydroxycamptothecin (SN-38). As a metabolite, SN-38 is formed by hydrolysis of irinotecan by carboxylesterases. In some embodiments, SN-38 has one of the following structures:



SN-38 has been described in U.S. patent application Ser. No. 7,999,083; U.S. patent application Ser. No. 8,080,250; U.S. patent application Ser. No. 8,759,496; U.S. patent application Ser. No. 8,999,344; U.S. patent application Ser. No. 10,195,288; and U.S. patent application Ser. No. 9,808,537.

[00109] In some embodiments, the camptothecin analog is exatecan methanesulfonate. Exatecan methanesulfonate (exatecan mesylate) is a water-soluble camptothecin (CPT) that exhibits more potent topoisomerase I inhibitory activity and antitumor activity than other CPT analogs. In addition, exatecan is effective against p-glycoprotein (P-gp)-mediated multi-drug resistant cells.

[00110] In some embodiments, the camptothecin analog is deruxtecan (Dxd), a potent derivative of exatecan, which has 10-fold higher topoisomerase I inhibitory potency than SN-38. In some embodiments, Dxd has the following structure:



Dxd has been described in U.S. patent application Ser. No. 6,407,115; U.S. patent application Ser. No. 10,195,288; U.S. patent application Ser. No. 9,808,537; and U.S. patent application Ser. No. 6,407,115.

[00111] The preparation of numerous compounds of the camptothecin analog class (including pharmaceutically acceptable salts, hydrates and solvates thereof) as well as the preparation of oral and parenteral pharmaceutical compositions comprising such a compounds of the camptothecin analog class and an inert, pharmaceutically acceptable carrier or diluent, is extensively described in U.S. Pat. No. 5,004,758, issued on Apr. 2, 1991 and European Patent Application Number 88311366.4, published on Jun. 21, 1989 as Publication Number EP 0 321 122, the teachings of which are incorporated herein by reference.

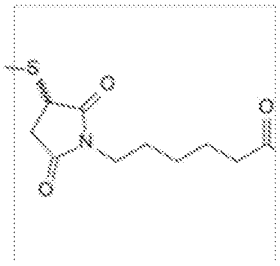
[00112] In still yet other embodiments of the invention, the chemotherapeutic agent is an antibiotic compound. Suitable antibiotics include, but are not limited to, doxorubicin, mitomycin, bleomycin, daunorubicin and streptozocin.

[00113] In some embodiments, the chemotherapeutic agent is an antimitotic alkaloid. In general, antimitotic alkaloids can be extracted from Cantharanthus roseus, and have been shown to be efficacious as anticancer chemotherapy agents. A great number of semi-synthetic derivatives have been studied both chemically and pharmacologically (see, O. Van Tellingen et al, Anticancer Research, 12, 1699-1716 (1992)). The antimitotic alkaloids of the present invention include, but are not limited to, vinblastine, vincristine, vindesine, Taxol and vinorelbine. The latter two antimitotic alkaloids are commercially available from Eli Lilly and Company, and Pierre Fabre Laboratories, respectively (see, U.S. Pat. No. 5,620,985). In one embodiment, the antimitotic alkaloid is vinorelbine.

[00114] In other embodiments of the invention, the chemotherapeutic agent is a difluoronucleoside. 2'-deoxy-2',2'-difluoronucleosides are known in the art as having antiviral activity. Such compounds are disclosed and taught in U.S. Pat. Nos. 4,526,988 and 4,808614. European Patent Application Publication 184,365 discloses that these same difluoronucleosides have oncolytic activity. In certain aspects, the 2'-deoxy-2',2'-difluoronucleoside used in the compositions and methods of the present invention is 2'-deoxy-2',2'-difluorocytidine hydrochloride, also known as gemcitabine hydrochloride. Gemcitabine is commercially available or can be synthesized in a multi-step process as disclosed and taught in U.S. Pat. Nos. 4,526,988, 4,808,614 and 5,223,608, the teachings of which are incorporated herein by reference.

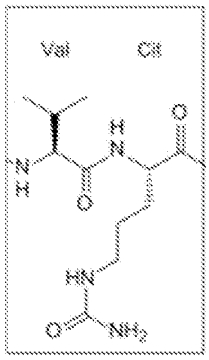
[00115] In various aspects, the chemotherapeutic agent is an anti-mitotic agent which inhibits cell division by blocking tubulin polymerization, destabilizing microtubules, or altering microtubule dynamics, *e.g.,* maytansinoid or a derivative thereof (*e.g.,* DM1 or DM4), auristatin or a derivative thereof. In various instances, the chemotherapeutic agent is an auristatin. For instance, the auristatin is in some aspects, dolastatin, Monomethyl auristatin E (MMAE), Monomethyl auristatin F (MMAF), or PF-06380101. Auristatins are described in the art. See, e.g., Maderna, A.; *et al.*, Mol Pharmaceutics 12(6): 1798-1812 (2015). In various aspects, the conjugate comprises an antibody of the present disclosure in combination with MMAE. Optionally, the conjugate comprises a linker. In some aspects, the linker comprises a cleavable linking moiety. In various instances, the conjugate comprises an antibody of the present disclosure linked to an attachment group which is

linked to a cathepsin-cleavable linker, which in turn is linked to a spacer which is linked to MMAE. In aspects, the attachment group is attached to the antibody via a Cys residue of the Fc region of the antibody. In exemplary aspects, the attachment group comprises the structure of Formula I:



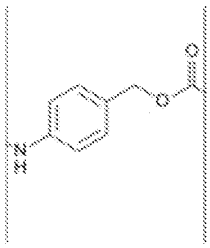
[Formula I]

In exemplary aspects, the cathepsin cleavable linker comprises the structure of Formula II:



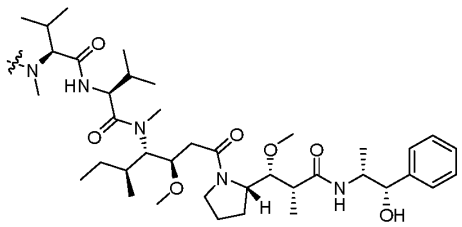
[Formula II].

In exemplary aspects, the spacer comprises the structure of Formula III:



[Formula III].

[00116] In some embodiments, MMAE has the following structure:



[00117] The present disclosure also provides conjugates comprising an antigen-binding protein of the present disclosure linked to a polypeptide, such that the conjugate is a fusion protein. Therefore, the present disclosure provides fusion proteins comprising an antigen-binding protein of the present disclosure linked to a polypeptide. In various embodiments, the polypeptide is a diagnostic label, e.g., a fluorescent protein, such as green fluorescent protein, or other tag, e.g., Myc tag. In various aspects, the polypeptide is one of the cytokines, lymphokines, growth factors, or other hematopoietic factors listed above.

[00118] The antigen-binding proteins of the present disclosure may be labeled with radionuclide for diagnostic or therapeutic purposes. Radionuclides that may be used to label the antigen-binding proteins include, but are not limited to, actinium-225 (^{225}Ac), astatine-211 (^{211}At), bismuth-213 (^{213}Bi), carbon-11 (^{11}C), copper-64 (^{64}Cu), fluorine-18 (^{18}F), gallium-68 (^{68}Ga), indium-111 (^{111}In), iodine-123 (^{123}I), iodine-124 (^{124}I), iodine-131 (^{131}I), lead-212 (^{212}Pb), lutetium-177 (^{177}Lu), radium-223 (^{223}Ra), technetium-99m (^{99m}Tc), thorium-227 (^{227}Th), yttrium-86 (^{86}Y), yttrium-90 (^{90}Y), and zirconium-89 (^{89}Zr). Radionuclides useful for SPECT imaging include gamma (γ)-ray emitters such as ^{123}I and ^{99m}Tc. Radionuclides useful for PET imaging include positron emitters such as ^{11}C, ^{18}F and ^{68}Ga. For therapeutic purposes, antigen-binding proteins labeled with alpha- (α-) and beta- (β-) particle emitters may be used. Alpha-particle emitters include ^{225}Ac, ^{213}Bi, ^{212}Pb, and ^{227Th}. Beta-particle emitters include ^{131}I , ^{177}Lu and ^{90}Y. In addition, both the α-particle and β-particle emitters may show fractional γ-ray emission and allow both imaging and therapy simultaneously. The antigen-binding proteins may be labeled separately with a radionuclide from a theranostic pair of radionuclides selected from the group consisting of $^{43/44}$Sc/^{47}Sc, ^{64}Cu/^{67}Cu, ^{83}Sr/^{89}Sr, ^{86}Y/^{90}Y, ^{110}In/^{111}In, ^{124}I/^{131}I, ^{152}Tb/^{161}Tb, ^{152}Tb/^{149}Tb, ^{68}Ga/^{177}Lu and ^{90}Y/^{177}Lu, and the pair of radiolabeled antigen-binding proteins may be used for both imaging and therapy. Alternatively, a single antigen-binding protein may be labeled with both radionuclides from a theranostic pair of radionuclides, and subsequently, used for both imaging and therapy. A number of radiolabeled antibodies in clinical trial for cancer imaging and treatment are provided in Parakh S, Lee ST, Gan HK, Scott AM. Radiolabeled Antibodies for Cancer Imaging and Therapy. *Cancers (Basel)*. 2022 Mar 11;14(6):1454. Labeling of proteins and antibodies with radionuclide is well known in the art (Gupta S, Batra S, Jain M. Antibody labeling with radioiodine and radiometals. *Methods Mol Biol.* 2014;1141:147-57; Sugiura G, Kühn H, Sauter M, Haberkorn U, Mier W. Radiolabeling strategies for tumor-targeting proteinaceous drugs. *Molecules.* 2014 Feb 18;19(2):2135-65;

Chomet M, van Dongen GAMS, Vugts DJ. State of the Art in Radiolabeling of Antibodies with Common and Uncommon Radiometals for Preclinical and Clinical Immuno-PET. *Bioconjugate Chemistry* 2021;32 (7):1315-1330; Kręcisz P, Czarnecka K, Krolicki L, Mikiciuk-Olasik E, Szymanski P. Radiolabeled Peptides and Antibodies in Medicine. *Bioconjugate Chem*. 2021:32:25−42; and Holik HA, Ibrahim FM, Elaine AA, Putra BD, Achmad A, Kartamihardja AHS. The Chemical Scaffold of Theranostic Radiopharmaceuticals: Radionuclide, Bifunctional Chelator, and Pharmacokinetics Modifying Linker. *Molecules*. 2022;27(10):3062).

[00119] *Linkers*

[00120] In some embodiments, the conjugate is directly linked to the heterologous moiety. In alternative embodiments, the conjugate comprises a linker that joins the compound of the present disclosure to the heterologous moiety. In some aspects, the linker comprises a chain of atoms from 1 to about 60, or 1 to 30 atoms or longer, 2 to 5 atoms, 2 to 10 atoms, 5 to 10 atoms, or 10 to 20 atoms long. In some embodiments, the chain atoms are all carbon atoms. In some embodiments, the chain atoms in the backbone of the linker are selected from the group consisting of C, O, N, and S. Chain atoms and linkers can be selected according to their expected solubility (hydrophilicity) so as to provide a more soluble conjugate. In some embodiments, the linker provides a functional group that is subject to cleavage by an enzyme or other catalyst or hydrolytic conditions found in the target tissue or organ or cell. In some embodiments, the length of the linker is long enough to reduce the potential for steric hindrance. In some embodiments, the linker is an amino acid or a peptidyl linker. Such peptidyl linkers can be any length. Various linkers are from about 1 to 50 amino acids in length, 5 to 50, 3 to 5, 5 to 10, 5 to 15, or 10 to 30 amino acids in length.

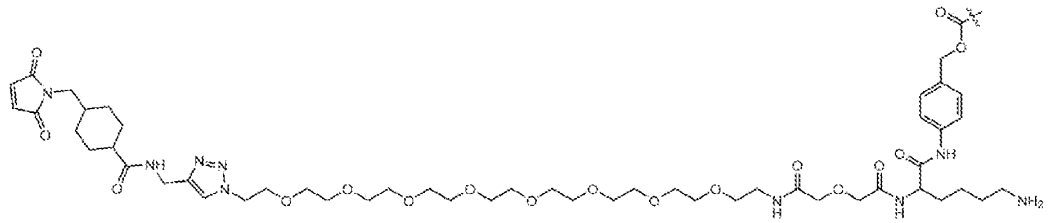
[00121] A variety of suitable linkers are known in the art. The linker can be cleavable (a cleavable linker), e.g., under physiological conditions, e.g., under intracellular conditions, such that cleavage of the linker releases the drug in the intracellular environment. Alternatively, the linker can be cleavable under extracellular conditions, *e.g.,* outside the tumor cells or in the vicinity of the tumor mass, such that cleavage of the linker releases the drug that permeates preferentially inside the tumor cells. In other embodiments, the linker is not cleavable (a non-cleavable linker), and the drug is released, for example, by antibody degradation.

[00122] The linker can be bonded to a chemically reactive group on the antibody moiety, e.g., to a free amino, imino, hydroxyl, thiol, or carboxyl group (e.g., to the N- or C-terminus, to the epsilon amino group of one or more lysine residues, to the free carboxylic acid group of one or more glutamic acid or aspartic acid residues, to the sulfhydryl group of one or more cysteinyl residues, or to the hydroxyl group of one or more serine or threonine residues). The site to which the linker is bound can be a natural residue in the amino acid sequence of the antibody moiety, or it can be introduced into the antibody moiety, e.g., by DNA recombinant technology (e.g., by introducing a cysteine or protease cleavage site in the amino acid sequence) or by protein biochemistry (e.g., reduction, pH adjustment, or proteolysis). The site to which the linker is bound can also be a non-natural amino acids. The site to which the linker is bound can also be a glycan on the antibody.

[00123] Typically, the linker is substantially inert under conditions for which the two groups it is connecting are linked. The term "bifunctional crosslinking agent," "bifunctional linker" or "crosslinking agent" refers to a modifying agent that possess two reactive groups at each end of the linker, such that one reactive group can be first reacted with the cytotoxic compound to provide a compound bearing the linker moiety and a second reactive group, which can then react with the antibody. Alternatively, one end of the bifunctional crosslinking agent can be first reacted with the antibody to provide an antibody bearing a linker moiety and a second reactive group, which can then react with the cytotoxic compound. The linking moiety may contain a chemical bond that allows for the release of the cytotoxic moiety at a particular site. Suitable chemical bonds are well known in the art and include disulfide bonds, thioether bonds, acid labile bonds, photolabile bonds, protease/peptidase labile bonds, and esterase labile bonds. See, for example, U.S. Patent Nos. 5,208,020; 5,475,092; 6,441,163; 6,716,821; 6,913,748; 7,276,497; 7,276,499; 7,368,565; 7,388,026 and 7,414,073. In some embodiments, the bonds are disulfide bonds, thioether, and/or protease/peptidase labile bonds. Other linkers that can be used in the present invention include non-cleavable linkers, such as those described in detail in US 20050169933, charged linkers, or hydrophilic linkers, such as those described in US 2009/0274713, US 2010/0129314, and WO 2009/134976, each of which is expressly incorporated herein by reference.

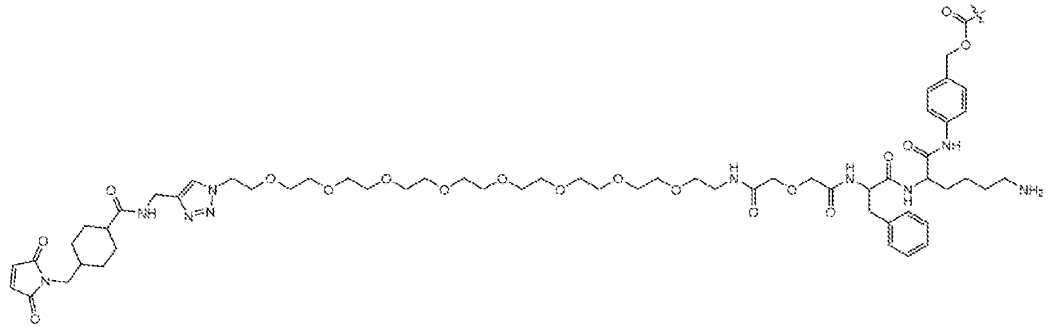
[00124] In some embodiments, the linker is a hydrophilic linker that confers hydrophilicity to the conjugate. In some embodiments, the hydrophilic linker comprises polyethylene glycol (PEG). In some embodiments, the hydrophilic linker comprises a

reactive maleimide functional group that can react with a free sulfhydryl group, such as in a cysteine to form a thioether bond. In some embodiments, the hydrophilic linker is CL2A. In some embodiments, the CL2A linker has the following structure:



CL2A has been described in U.S. Patent Nos. 8,080,250; 8,759,496; and 10,195,288.

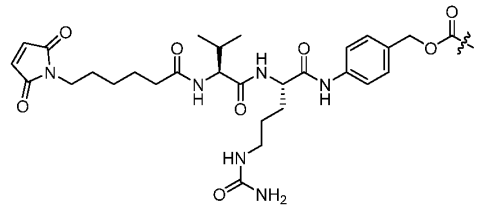
[00125] In some embodiments, the hydrophilic linker is CL2E. In some embodiments, the CL2E comprises a reactive maleimide functional group at one end and has the following structure:



CL2E has been described in U.S. Patent Nos. 8,080,250; 8,759,496; and 10,195,288.

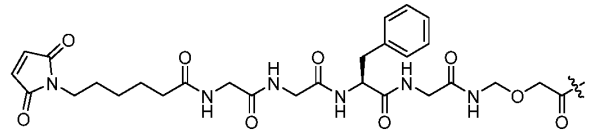
[00126] In some embodiments, the linker is cleavable by a cleaving agent that is present in the intracellular environment (e.g., within a lysosome or endosome or caveolae). The linker can be, e.g., a peptide linker that is cleaved by an intracellular or extracellular peptidase or protease enzyme, including, but not limited to, a lysosomal or endosomal protease. In some embodiments, the peptide linker comprises at least two, at least three, at least four, or at least five amino acids long.

[00127] In some embodiments, the peptide linker comprises VC-PAB, comprising valine and citrulline residues followed by the ρ-aminobenzyl group (valine-citrulline-ρ-aminobenzyl group). In some embodiments, the VC-PAB further comprises a maleimide group (MC-VC-PAB) and can have the following structure:



VC-PAB and MC-VC-PAB have been described in U.S. Patent Nos. 7,659,241; 7,829,531; 6,884,869; 6,214,345; and 6,214,345.

[00128] In some embodiments, the peptide linker comprises glycine-glycine-phenylalanine-glycine (GGFG). In some such embodiments, the linker is maleimidocaproyl glycine-glycine-phenylalanine-glycine (MC-GGFG). In some embodiments, the MC-GGFG linker has the following structure:



GGFG and MC-GGFG have been described in U.S. Patent Nos. 9,808,537 and 10,195,288.

[00129] In other embodiments, the cleavable linker is pH-sensitive, i.e., sensitive to hydrolysis at certain pH values. In some embodiments, the pH-sensitive linker is hydrolyzable under acidic conditions. For example, an acid-labile linker that is hydrolyzable in the lysosome (e.g., a hydrazone, semicarbazone, thiosemicarbazone, cis-aconitic amide, ortho ester, acetal, ketal, or the like) can be used (see, e.g., US Patent Nos. 5,122,368; 5,824,805; 5,622,929; Dubowchik and Walker, 1999, Pharm. Therapeutics 83:67-123; Neville et al, 1989, Biol. Chem. 264: 14653-14661). Such linkers are relatively stable under neutral pH conditions, such as those in the blood, but are unstable at below pH 5.5 or 5.0, the approximate pH of the lysosome. In certain embodiments, the hydrolyzable linker is a thioether linker (such as, e.g., a thioether attached to the therapeutic agent via an acylhydrazone bond (see, e.g., US Patent No. 5,622,929).

[00130] In other embodiments, the linker is cleavable under reducing conditions (e.g., a disulfide linker). Bifunctional crosslinking agents that enable the linkage of an antibody with cytotoxic compounds via disulfide bonds include, but are not limited to, N-succinimidyl-4-(4-nitropyridyl-2-dithio)butanoate, N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), N-succinimidyl-4-(2-pyridyldithio)pentanoate (SPP), N-succinimidyl-4-(2-pyridyldithio)butanoate (SPDB), N-succinimidyl-4-(2-pyridyldithio)-2-sulfo butanoate (sulfo-SPDB). Sulfo-SPDB is described, e.g., in US Patent 8,236,319, incorporated herein by reference. Alternatively, crosslinking agents that introduce thiol

groups such as 2-iminothiolane, homocysteine thiolactone, or S-acetylsuccinic anhydride can be used. In other embodiments, the linker may contain a combination of one or more of the peptide, pH-sensitive, or disulfide linkers described previously.

[00131] "Heterobifunctional crosslinking agents" are bifunctional crosslinking agents having two different reactive groups. Heterobifunctional crosslinking agents containing both an amine-reactive N-hydroxysuccinimide group (NHS group) and a carbonyl-reactive hydrazine group can also be used to link cytotoxic compounds with an antibody. Examples of such commercially available heterobifunctional crosslinking agents include succinimidyl 6-hydrazinonicotinamide acetone hydrazone (SANH), succinimidyl 4-hydrazidoterephthalate hydrochloride (SHTH) and succinimidyl hydrazinium nicotinate hydrochloride (SHNH). Conjugates bearing an acid-labile linkage can also be prepared using a hydrazine-bearing benzodiazepine derivative of the present invention. Examples of bifunctional crosslinking agents that can be used include succinimidyl-p-formyl benzoate (SFB) and succinimidyl-p-formylphenoxyacetate (SFPA).

[00132] The linkers described herein may be used in any combination with the heterologous moiety described herein. In addition, the linkers described herein can have any chemical reactive moieties (e.g., maleimide, cysteine, etc.) that can react with any part (e.g., an amino acid, disulfide bond, carbohydrate (e.g., those from the post-translational modification), etc.) of the antigen-binding protein of the present disclosure. Often, lysines or cysteines (e.g., cysteines from the reduced disulfide bonds (e.g., from interchain or intrachain disulfide bonds of the antibody or antigen-binding protein) or an engineered unpaired cysteine) on an antibody or an antigen-binding protein have been used as a site for conjuation. All of the above-listed linkers and heterologous moiety described herein are available commercially and/or can be prepared by conventional techniques including those described in the above-listed references.

[00133] *Conjugation*

[00134] The heterologous moiety-to-antigen-binding protein ratio (HAR) represents the number of a heterologous moiety linked per antigen-binding molecule. In some embodiments, the HAR ranges from 1 to 15, 1 to 10, 1 to 9, 1 to 8, 1 to 7, 1 to 6, 1 to 5, 1 to 4, 1 to 3, or 1 to 2. In some embodiments, the HAR ranges from 2 to 10, 2 to 9, 2 to 8, 2 to 7, 2 to 6, 2 to 5, 2 to 4 or 2 to 3. In other embodiments, the HAR is about 2, about 2.5, about 3, about 4, about 5, or about 6. In some embodiments, the HAR ranges from about 2

to about 4. The HAR may be characterized by conventional means such as mass spectrometry, UV/Vis spectroscopy, ELISA assay, and/or HPLC.

[00135] In some embodiments, the conjugates are heterogeneous conjugates (also referred to as "conventional"), wherein the antigen-binding proteins are conjugated to a different number of the heterologous moiety. In some embodiments, the heterogeneous conjugates follow a Gaussian distribution or quasi-Gaussian distribution of the conjugates, wherein the distribution centers on the average heterologous moiety loading value with some antigen-binding proteins conjugated with higher than average and some antigen-binding proteins conjugated with lower than the average.

[00136] In some embodiments, the conjugates are homogeneous conjugates, wherein the substantial percentage of the antigen-binding proteins are conjugated to a defined number of the heterologous moiety. In some embodiments, the homogeneous conjugates comprise the HAR of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10. In some embodiments, the homogeneous conjugates comprise the HAR of 2, 4, 6, or 8. In preferred embodiments, the homogeneous conjugates comprise the HAR of 4. In other preferred embodiments, the homogeneous conjugates comprise the HAR of 2. In some embodiments, the homogeneous conjugates comprise greater than or equal to 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 percent conjugates with the defined HAR. In some embodiments, the homogeneous conjugates comprise about 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 percent conjugates with the defined HAR. In some embodiments, the homogeneous conjugates comprise at least 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 percent conjugates with the defined HAR. In some embodiments, the homogeneous conjugates comprise the HAR distribution that is not Gaussian or quasi-Gaussian distribution. In some embodiments, the homogeneity of the homogeneous conjugates is determined by a chromatogram, *e.g.,* HPLC or any suitable chromatography. In some embodiments, the chromatogram is a HIC chromatogram. The homogeneous conjugate may be generated by a site-specific conjugation.

[00137] In some embodiments, the heterologous moiety is conjugated to the antigen-binding protein (e.g., antibody) in a site-specific manner. Various site-specific conjugation methods are known in the art, e.g., thiomab or TDC or conjugation at an unpaired cysteine residue (Junutula *et al.* (2008) *Nat. Biotechnol.* 26:925-932; Dimasi *et al.* (2017) *Mol.*

Pharm. 14:1501-1516; Shen *et al.* (2012) *Nat. Biotechnol.* 30:184-9); thiol bridge linker (Behrens *et al.* (2015) *Mol. Pharm.* 12:3986-98); conjugation at glutamine using a transglutaminase (Dennler *et al.* (2013) *Methods Mol. Bio.* 1045:205-15; Dennler *et al.* (2014) *Bioconjug Chem.* 25:569-78); conjugation at engineered unnatural amino acid residues (Axup *et al.* (2012) *Proc Natl Acad Sci U.S.A.* 104-16101-6; Tian *et al.* (2014) *Proc Natl Acad Sci U.S.A.* 111:1766-71; VanBrunt *et al.* (2015) *Bioconjug Chem* 26:2249-60; Zimmerman *et al.* (2014) *Bioconjug Chem* 25:351-61); selenocysteine conjugation (Li *et al.* (2017) *Cell Chem Biol* 24:433-442); glycan-mediated conjugation (Okeley *et al.* (2013) *Bioconjug Chem* 24:1650-5); conjugation at galactose or GalNAc analogues (Ramakrishnan and Qasba (2002) *J Biol Chem* 277:20833-9; van Geel *et al.* (2015) *Bioconjug Chem* 26:2233-42); via glycan engineering (Zhou *et al.* (2014) *Bioconjug Chem* 25:510-20; Tang *et al.* (2017) *Nat Protoc* 12:1702-1721); via a short peptide tag, such as engineering a glutamine tag or sortase A-mediated transpeptidation (Strop *et al.* (2013) *Chem Biol* 20:161-7; Beerli *et al.* (2015) *PLoS One* 10:e0131177); and via an aldehyde tag (Wu *et al.* (2009) *Proc Natl Acad Sci U.S.A.* 106:3000-5).

[00138] *Compositions, Pharmaceutical Compositions and Formulations*

[00139] Compositions comprising an antigen-binding protein, a nucleic acid, a vector, a host cell, or a conjugate as presently disclosed are provided herein. The compositions in some aspects comprise the antigen-binding proteins in isolated and/or purified form. In some aspects, the composition comprises a single type (e.g., structure) of an antigen-binding protein of the present disclosure or comprises a combination of two or more antigen-binding proteins of the present disclosure, wherein the combination comprises two or more antigen-binding proteins of different types (e.g., structures).

[00140] In some aspects, the composition comprises agents which enhance the chemico-physico features of the antigen-binding protein, e.g., via stabilizing the antigen-binding protein at certain temperatures, e.g., room temperature, increasing shelf life, reducing degradation, e.g., oxidation, protease mediated degradation, increasing half-life of the antigen-binding protein, etc. In some aspects, the composition comprises any of the agents disclosed herein as a heterologous moiety or conjugate moiety, optionally in admixture with the antigen-binding proteins of the present disclosure or conjugated to the antigen-binding proteins.

[00141] In various aspects of the present disclosure, the composition additionally comprises a pharmaceutically acceptable carrier, diluents, or excipient. In some

embodiments, the antigen-binding protein, a nucleic acid, a vector, a host cell, or a conjugate as presently disclosed (hereinafter referred to as "active agents") is formulated into a pharmaceutical composition comprising the active agent, along with a pharmaceutically acceptable carrier, diluent, or excipient. In this regard, the present disclosure further provides pharmaceutical compositions comprising an active agent which is intended for administration to a subject, e.g., a mammal.

[00142] In some embodiments, the active agent is present in the pharmaceutical composition at a purity level suitable for administration to a patient. In some embodiments, the active agent has a purity level of at least about 90%, about 91%, about 92%, about 93%, about 94%, about 95%, about 96%, about 97%, about 98% or about 99%, and a pharmaceutically acceptable diluent, carrier or excipient. In some embodiments, the compositions contain an active agent at a concentration of about 0.001 to about 30.0 mg/ml.

[00143] In various aspects, the pharmaceutical compositions comprise a pharmaceutically acceptable carrier. As used herein, the term "pharmaceutically acceptable carrier" includes any of the standard pharmaceutical carriers, such as a phosphate buffered saline solution, water, emulsions such as an oil/water or water/oil emulsion, and various types of wetting agents. The term also encompasses any of the agents approved by a regulatory agency of the US Federal government or listed in the US Pharmacopeia for use in animals, including humans.

[00144] The pharmaceutical composition can comprise any pharmaceutically acceptable ingredients, including, for example, acidifying agents, additives, adsorbents, aerosol propellants, air displacement agents, alkalizing agents, anticaking agents, anticoagulants, antimicrobial preservatives, antioxidants, antiseptics, bases, binders, buffering agents, chelating agents, coating agents, coloring agents, desiccants, detergents, diluents, disinfectants, disintegrants, dispersing agents, dissolution enhancing agents, dyes, emollients, emulsifying agents, emulsion stabilizers, fillers, film forming agents, flavor enhancers, flavoring agents, flow enhancers, gelling agents, granulating agents, humectants, lubricants, mucoadhesives, ointment bases, ointments, oleaginous vehicles, organic bases, pastille bases, pigments, plasticizers, polishing agents, preservatives, sequestering agents, skin penetrants, solubilizing agents, solvents, stabilizing agents, suppository bases, surface active agents, surfactants, suspending agents, sweetening agents, therapeutic agents, thickening agents, tonicity agents, toxicity agents, viscosity-increasing agents, water-absorbing agents, water-miscible cosolvents, water softeners, or wetting agents. *See, e.g.,*

the *Handbook of Pharmaceutical Excipients*, Third Edition, A. H. Kibbe (Pharmaceutical Press, London, UK, 2000), which is incorporated by reference in its entirety. *Remington's Pharmaceutical Sciences*, Sixteenth Edition, E. W. Martin (Mack Publishing Co., Easton, Pa., 1980), which is incorporated by reference in its entirety.

[00145] In various aspects, the pharmaceutical composition comprises formulation materials that are nontoxic to recipients at the dosages and concentrations employed. In specific embodiments, pharmaceutical compositions comprising an active agent and one or more pharmaceutically acceptable salts; polyols; surfactants; osmotic balancing agents; tonicity agents; antioxidants; antibiotics; antimycotics; bulking agents; lyoprotectants; anti-foaming agents; chelating agents; preservatives; colorants; analgesics; or additional pharmaceutical agents. In various aspects, the pharmaceutical composition comprises one or more polyols and/or one or more surfactants, optionally, in addition to one or more excipients, including but not limited to, pharmaceutically acceptable salts; osmotic balancing agents (tonicity agents); antioxidants; antibiotics; antimycotics; bulking agents; lyoprotectants; anti-foaming agents; chelating agents; preservatives; colorants; and analgesics.

[00146] In certain embodiments, the pharmaceutical composition can contain formulation materials for modifying, maintaining or preserving, for example, the pH, osmolarity, viscosity, clarity, color, isotonicity, odor, sterility, stability, rate of dissolution or release, adsorption or penetration of the composition. In such embodiments, suitable formulation materials include, but are not limited to, amino acids (such as glycine, glutamine, asparagine, arginine or lysine); antimicrobials; antioxidants (such as ascorbic acid, sodium sulfite or sodium hydrogen-sulfite); buffers (such as borate, bicarbonate, Tris-HCl, citrates, phosphates or other organic acids); bulking agents (such as mannitol or glycine); chelating agents (such as ethylenediamine tetraacetic acid (EDTA)); complexing agents (such as caffeine, polyvinylpyrrolidone, beta-cyclodextrin or hydroxypropyl-beta-cyclodextrin); fillers; monosaccharides; disaccharides; and other carbohydrates (such as glucose, mannose or dextrins); proteins (such as serum albumin, gelatin or immunoglobulins); coloring, flavoring and diluting agents; emulsifying agents; hydrophilic polymers (such as polyvinylpyrrolidone); low molecular weight polypeptides; salt-forming counterions (such as sodium); preservatives (such as benzalkonium chloride, benzoic acid, salicylic acid, thimerosal, phenethyl alcohol, methylparaben, propylparaben, chlorhexidine, sorbic acid or hydrogen peroxide); solvents (such as glycerin, propylene glycol or

polyethylene glycol); sugar alcohols (such as mannitol or sorbitol); suspending agents; surfactants or wetting agents (such as pluronics, PEG, sorbitan esters, polysorbates such as polysorbate 20, polysorbate, triton, tromethamine, lecithin, cholesterol, tyloxapol); stability enhancing agents (such as sucrose or sorbitol); tonicity enhancing agents (such as alkali metal halides, preferably sodium or potassium chloride, mannitol, sorbitol, and/or dextrose); delivery vehicles; diluents; excipients and/or pharmaceutical adjuvants. See, REMINGTON'S PHARMACEUTICAL SCIENCES, 18″ Edition, (A. R. Gennaro, ed.), 1990, Mack Publishing Company.

[00147] The pharmaceutical compositions can be formulated to achieve a physiologically compatible pH. In some embodiments, the pH of the pharmaceutical composition can be for example between about 4 or about 5 and about 8.0 or about 4.5 and about 7.5 or about 5.0 to about 7.5. In various embodiments, the pH of the pharmaceutical composition is between 5.5 and 7.5.

[00148] The present disclosure provides methods of producing a pharmaceutical composition. In various aspects, the method comprises combining the antigen-binding protein, conjugate, fusion protein, nucleic acid, vector, host cell, or a combination thereof, with a pharmaceutically acceptable carrier, diluent, or excipient.

[00149] *Routes of Administration*

[00150] With regard to the present disclosure, the active agent, or pharmaceutical composition comprising the same, can be administered to the subject via any suitable route of administration. For example, the active agent can be administered to a subject via parenteral, nasal, oral, pulmonary, topical, vaginal, or rectal administration. The following discussion on routes of administration is merely provided to illustrate various embodiments and should not be construed as limiting the scope in any way.

[00151] Formulations suitable for parenteral administration include aqueous and non-aqueous, isotonic sterile injection solutions, which can contain antioxidants, buffers, bacteriostats, and solutes that render the formulation isotonic with the blood of the intended recipient, and aqueous and non-aqueous sterile suspensions that can include suspending agents, solubilizers, thickening agents, stabilizers, and preservatives. The term, "parenteral" means not through the alimentary canal but by some other route such as subcutaneous, intramuscular, intraspinal, or intravenous. The active agent of the present disclosure can be administered with a physiologically acceptable diluent in a pharmaceutical carrier, such as a sterile liquid or mixture of liquids, including water, saline,

aqueous dextrose and related sugar solutions, an alcohol, such as ethanol or hexadecyl alcohol, a glycol, such as propylene glycol or polyethylene glycol, dimethylsulfoxide, glycerol, ketals such as 2,2- dimethyl-l,3-dioxolane-4-methanol, ethers, polyethylene glycol 400, oils, fatty acids, fatty acid esters or glycerides, or acetylated fatty acid glycerides with or without the addition of a pharmaceutically acceptable surfactant, such as a soap or a detergent, suspending agent, such as pectin, carbomers, methylcellulose, hydroxypropylmethylcellulose, or carboxymethylcellulose, or emulsifying agents and other pharmaceutical adjuvants.

[00152] Oils, which can be used in parenteral formulations include petroleum, animal, vegetable, or synthetic oils. Specific examples of oils include peanut, soybean, sesame, cottonseed, corn, olive, petrolatum, and mineral. Suitable fatty acids for use in parenteral formulations include oleic acid, stearic acid, and isostearic acid. Ethyl oleate and isopropyl myristate are examples of suitable fatty acid esters.

[00153] Suitable soaps for use in parenteral formulations include fatty alkali metal, ammonium, and triethanolamine salts, and suitable detergents include (a) cationic detergents such as, for example, dimethyl dialkyl ammonium halides, and alkyl pyridinium halides, (b) anionic detergents such as, for example, alkyl, aryl, and olefin sulfonates, alkyl, olefin, ether, and monoglyceride sulfates, and sulfosuccinates, (c) nonionic detergents such as, for example, fatty amine oxides, fatty acid alkanolamides, and polyoxyethylene-polypropylene copolymers, (d) amphoteric detergents such as, for example, alkyl-β-aminopropionates, and 2-alkyl -imidazoline quaternary ammonium salts, and (e) mixtures thereof.

[00154] The parenteral formulations in some embodiments contain from about 0.5% to about 25% by weight of the active agent of the present disclosure in solution. Preservatives and buffers can be used. In order to minimize or eliminate irritation at the site of injection, such compositions can contain one or more nonionic surfactants having a hydrophile-lipophile balance (HLB) of from about 12 to about 17. The quantity of surfactant in such formulations will typically range from about 5% to about 15% by weight. Suitable surfactants include polyethylene glycol sorbitan fatty acid esters, such as sorbitan monooleate and the high molecular weight adducts of ethylene oxide with a hydrophobic base, formed by the condensation of propylene oxide with propylene glycol. The parenteral formulations in some aspects are presented in unit-dose or multi-dose sealed containers, such as ampoules and vials, and can be stored in a freeze-dried (lyophilized) condition

requiring only the addition of the sterile liquid excipient, for example, water, for injections, immediately prior to use. Extemporaneous injection solutions and suspensions in some aspects are prepared from sterile powders, granules, and tablets of the kind previously described.

[00155] Injectable formulations are in accordance with the present disclosure. The requirements for effective pharmaceutical carriers for injectable compositions are well-known to those of ordinary skill in the art (see, e.g., *Pharmaceutics and Pharmacy Practice*, J. B. Lippincott Company, Philadelphia, PA, Banker and Chalmers, eds., pages 238-250 (1982), and *ASHP Handbook on Injectable Drugs*, Trissel, 4th ed., pages 622-630 (1986)).

[00156] *Dosages*

[00157] The active agents of the disclosure are believed to be useful in methods of inhibiting tumor growth, as well as other methods, as further described herein, including methods of treating or preventing cancer. For purposes of the disclosure, the amount or dose of the active agent administered should be sufficient to effect, e.g., a therapeutic or prophylactic response, in the subject or animal over a reasonable time frame. For example, the dose of the active agent of the present disclosure should be sufficient to treat cancer as described herein in a period of from about 1 to 4 minutes, 1 to 4 hours or 1 to 4 weeks or longer, e.g., 5 to 20 or more weeks, from the time of administration. In certain embodiments, the time period could be even longer. The dose will be determined by the efficacy of the particular active agent and the condition of the animal (e.g., human), as well as the body weight of the animal (e.g., human) to be treated.

[00158] Many assays for determining an administered dose are known in the art. For purposes herein, an assay, which comprises comparing the extent to which cancer is treated upon administration of a given dose of the active agent of the present disclosure to a mammal among a set of mammals, each set of which is given a different dose of the active agent, could be used to determine a starting dose to be administered to a mammal. The extent to which cancer is treated upon administration of a certain dose can be represented by, for example, the extent of tumor regression achieved with the active agent in a mouse xenograft model. Methods of assaying tumor regression are known in the art and described herein in EXAMPLES.

[00159] The dose of the active agent of the present disclosure also will be determined by the existence, nature and extent of any adverse side effects that might accompany the

administration of a particular active agent of the present disclosure. Typically, the attending physician will decide the dosage of the active agent of the present disclosure with which to treat each individual patient, taking into consideration a variety of factors, such as age, body weight, general health, diet, sex, active agent of the present disclosure to be administered, route of administration, and the severity of the condition being treated. By way of example and not intending to limit the present disclosure, the dose of the active agent of the present disclosure per administration can be about 2 mg to about 10 mg/kg body weight of the subject being treated. In an embodiment, the dose can be about 2 mg to about 3 mg/kg body weight of the subject being treated, about 2 mg to about 4 mg/kg body weight, about 2 mg to about 5 mg/kg body weight, about 2 mg to about 6 mg/kg body weight, about 2 mg to about 7 mg/kg body weight, 2 mg to about 8 mg/kg body weight, or about 2 mg to about 9 mg/kg body weight. In a separate embodiment, the dose can be about 2 mg to about 3 mg/kg body weight of the subject being treated. In a different embodiment, the dose can be about 3 mg to about 4 mg/kg body weight. In an embodiment, the dose can be about 4 mg to about 5 mg/kg body weight. In an embodiment, the dose can be about 5 mg to about 6 mg/kg body weight. In an embodiment, the dose can be about 6 mg to about 7 mg/kg body weight. In an embodiment, the dose can be about 7 mg to about 8 mg/kg body weight. In an embodiment, the dose can be about 8 mg to about 9 mg/kg body weight. In an embodiment, the dose can be about 9 mg to about 10 mg/kg body weight. In a preferred embodiment, the dose of the active agent of the present disclosure per administration can be about 2.4 mg to 3 mg/kg body weight of the subject being treated. In a preferred embodiment, the dose of the active agent per administration may be selected from the group consisting of about 2.4 mg/kg body weight, about 2.5 mg/kg body weight, about 2.6 mg/kg body weight, about 2.7 mg/kg body weight, about 2.8 mg/kg body weight, about 2.9 mg/kg body weight, and about 3.0 mg/kg body weight of the subject being treated. By way of example and not intending to limit the present disclosure, an interval between doses can be about 1 week, about 2 weeks, about 3 weeks, about 4 weeks or longer. The interval between doses may be adjusted depending on response of the subject to treatment. By way of example and not intending to limit the present disclosure, the average dose of the active agent of the present disclosure can be about 0.0001 to about 1 g/kg body weight of the subject being treated/day, from about 0.0001 to about 0.001 g/kg body weight/day, or about 0.01 mg to about 1 g/kg body weight/day. In some embodiment, the

average dose of the active agent of the present disclosure can be about 0.1 mg to about 0.01 mg to 1 mg/kg body weight/day.

[00160] *Controlled Release Formulations*

[00161] In some embodiments, the active agents described herein can be modified into a depot form, such that the manner in which the active agent of the present disclosure is released into the body to which it is administered is controlled with respect to time and location within the body (see, for example, U.S. Patent No. 4,450,150). Depot forms of active agents of the present disclosure can be, for example, an implantable composition comprising the active agents and a porous or non-porous material, such as a polymer, wherein the active agent is encapsulated by or diffused throughout the material and/or degradation of the non-porous material. The depot is then implanted into the desired location within the body of the subject and the active agent is released from the implant at a predetermined rate.

[00162] The pharmaceutical composition comprising the active agent in certain aspects is modified to have any type of *in vivo* release profile. In some aspects, the pharmaceutical composition is an immediate release, controlled release, sustained release, extended release, delayed release, or bi-phasic release formulation. Methods of formulating peptides for controlled release are known in the art. See, for example, Qian et al., *J Pharm* 374: 46-52 (2009) and International Patent Application Publication Nos. WO 2008/130158, WO2004/033036; WO2000/032218; and WO 1999/040942.

[00163] The instant compositions can further comprise, for example, micelles or liposomes, or some other encapsulated form, or can be administered in an extended-release form to provide a prolonged storage and/or delivery effect.

[00164] *Use*

[00165] The antigen-binding proteins of the present disclosure are useful for inhibiting proliferation of cancer cells and/or inhibiting tumor growth. Without being bound to a particular theory, the inhibiting action of the antigen-binding proteins provided herein allow such entities to be useful in methods of treating cancer.

[00166] Accordingly, provided herein are methods of inhibiting proliferation of cancer cells and/or inhibiting tumor growth in a subject and methods of reducing tumor size in a subject. In various embodiments, the methods comprise administering to the subject the pharmaceutical composition of the present disclosure in an amount effective for inhibiting tumor growth or reducing tumor size in the subject. In various aspects, the growth of a

P2RY8-associated or expressing tumor is inhibited. In various aspects, the size of a P2RY8-associated or expressing tumor is reduced. In various aspects, the any tumor or cancer includes any of B-cell neoplasms, thymic epithelial tumor, renal clear cell carcinoma, seminoma, miscellaneous neuroepithelial tumor, thyroid cancer, pheochromocytoma, pancreatic cancer, hepatobiliary cancer, sarcoma, non-seminomatous germ cell tumor, pleural mesothelioma, non-small cell lung cancer, melanoma, renal non-clear cell carcinoma, breast cancer, esophagogastric cancer, cholangiocarcinoma, prostate cancer, head and neck cancer, colorectal cancer, bladder cancer, cervical cancer, glioblastoma, ocular melanoma, ovarian epithelial tumor, endometrial cancer, glioma, a lymphoma, leukemia and myeloma where P2RY8 is expressed or overexpressed. In various aspects, the proliferation of a P2RY8-associated or expressing lymphoma, leukemia, or myeloma is inhibited. In various aspects, the proliferation of a P2RY8-associated lymphoma is inhibited. While leukemia, lymphoma, and myeloma are considered liquid tumors, in certain instances, said cancer indications develop a tumor mass. For example, acute myeloid leukemia develops extramedullary tumor mass (known as myeloid sarcoma) consisting of myeloid blasts which efface the tissue architecture. In some such instances, the antigen-binding proteins and/or compositions of the present disclosure are effective in reducing the size of such tumor mass.

[00167] As used herein, the term "inhibit" or "reduce" and words stemming therefrom may not be a 100% or complete inhibition or reduction. Rather, there are varying degrees of inhibition or reduction of which one of ordinary skill in the art recognizes as having a potential benefit or therapeutic effect. In this respect, the antigen-binding proteins of the present disclosure may inhibit tumor growth or reduce tumor size to any amount or level. In various embodiments, the inhibition provided by the methods of the present disclosure is at least or about a 10% inhibition (e.g., at least or about a 20% inhibition, at least or about a 30% inhibition, at least or about a 40% inhibition, at least or about a 50% inhibition, at least or about a 60% inhibition, at least or about a 70% inhibition, at least or about a 80% inhibition, at least or about a 90% inhibition, at least or about a 95% inhibition, at least or about a 98% inhibition). In various embodiments, the reduction provided by the methods of the present disclosure is at least or about a 10% reduction (e.g., at least or about a 20% reduction, at least or about a 30% reduction, at least or about a 40% reduction, at least or about a 50% reduction, at least or about a 60% reduction, at least or about a 70% reduction,

at least or about a 80% reduction, at least or about a 90% reduction, at least or about a 95% reduction, at least or about a 98% reduction).

[00168] Additionally provided herein are methods of treating a subject with cancer, e.g., P2RY8-expressing cancer. In various embodiments, the method comprises administering to the subject the pharmaceutical composition of the present disclosure in an amount effective for treating the cancer in the subject.

[00169] An "effective amount" of a substance (e.g., antibody, cell, etc.) is an amount capable of producing a medically desirable result in a treated patient, e.g., decrease tumor burden, decrease the growth of tumor cells, or alleviate any symptom associated with cancer, with an acceptable benefit: risk ratio, preferably in a human or non-human mammal.

[00170] For purposes herein, the cancer of the methods disclosed herein can be any cancer, e.g., any malignant growth or tumor caused by abnormal and uncontrolled cell division that may spread to other parts of the body through the lymphatic system or the blood stream, preferably where the cancer is associated with aberrant P2RY8 protein expression. In some embodiments, the cancer is associated with overexpression of P2RY8 protein. In some embodiments, the cancer is associated with expression of a mutant P2RY8 protein. The cancer in some aspects is one selected from the group consisting of acute lymphocytic cancer, acute myeloid leukemia, alveolar rhabdomyosarcoma, bone cancer, brain cancer, breast cancer, cancer of the anus, anal canal, or anorectum, cancer of the eye, cancer of the intrahepatic bile duct, cancer of the joints, cancer of the neck, gallbladder, or pleura, cancer of the nose, nasal cavity, or middle ear, cancer of the oral cavity, cancer of the vulva, chronic lymphocytic leukemia, chronic myeloid cancer, colon cancer, esophageal cancer, cervical cancer, gastrointestinal carcinoid tumor, Hodgkin lymphoma, hypopharynx cancer, kidney cancer, larynx cancer, liver cancer, lung cancer, malignant mesothelioma, melanoma, multiple myeloma, nasopharynx cancer, non-Hodgkin lymphoma, ovarian cancer, pancreatic cancer, peritoneum, omentum, and mesentery cancer, pharynx cancer, prostate cancer, rectal cancer, renal cancer (e.g., renal cell carcinoma (RCC)), small intestine cancer, soft tissue cancer, stomach cancer, testicular cancer, thyroid cancer, ureter cancer, and urinary bladder cancer. In particular aspects, the cancer is a lymphoma, leukemia, myeloma, mature B-cell neoplasms, thymic epithelial tumor, renal clear cell carcinoma, serinoma, miscellaneous neuroepithelial tumor, thyroid cancer, pheochromocytoma, pancreatic cancer, hepatobiliary cancer, sarcoma, non-seminomatous germ cell tumor, pleural mesothelioma, non-small cell lung cancer, melanoma, renal non-

clear cell carcinoma, breast cancer, esophagogastric cancer, cholangiocarcinoa, prostate cancer, head and neck cancer, colorectal cancer, bladder cancer, cervical cancer, glioblastoma, ocular melanoma, ovarian epithelial tumor, endometrial cancer or glioma. In various aspects, the cancer is any cancer characterized by moderate to high expression of P2RY8. See, e.g., Figs. 1 (A-100) and 2 (A-200). In various aspects, the cancer comprises an altered expression of the P2RY8 gene, either overexpression of P2RY8 gene or expression of a mutant P2RY8 gene. In particular aspects, the myeloma is multiple myeloma. In particular aspects, the leukemia is acute myeloid leukemia (AML). In particular aspects, the AML is any of AML with defining genetic abnormalities, AML with differentiation, myeloid sarcoma and secondary myeloid neoplasms. In particular aspects, the leukemia is acute lymphoblastic leukemia. In particular aspects, the lymphoma is non-Hodgkin lymphoma. In particular aspects, the non-Hodgkin lymphoma is any of diffuse large B cell lymphoma, follicular lymphoma, mantle cell lymphoma, marginal zone lymphoma, chronic lymphocytic leukemia/small lymphocytic lymphoma (CLL/SLL), and lymphoplasmacytic lymphoma.

[00171] As used herein, the term "treat," as well as words related thereto, do not necessarily imply 100% or complete treatment. Rather, there are varying degrees of treatment of which one of ordinary skill in the art recognizes as having a potential benefit or therapeutic effect. In this respect, the methods of treating cancer of the present disclosure can provide any amount or any level of treatment. Furthermore, the treatment provided by the method of the present disclosure can include treatment of one or more conditions or symptoms or signs of the cancer being treated. Also, the treatment provided by the methods of the present disclosure can encompass slowing the progression of the cancer. For example, the methods can treat cancer by virtue of enhancing the T cell activity or an immune response against the cancer, reducing tumor or cancer growth, reducing metastasis of tumor cells, increasing cell death of tumor or cancer cells, and the like. In various aspects, the methods treat by way of delaying the onset or recurrence of the cancer by, e.g., at least 1 day, 2 days, 4 days, 6 days, 8 days, 10 days, 15 days, 30 days, two months, 3 months, 4 months, 6 months, 1 year, 2 years, 3 years, 4 years, or more. In various aspects, the methods treat by way increasing the survival of the subject.

[00172] The antigen binding proteins of the present disclosure also may be used to detect P2RY8 in a sample or diagnose a P2RY8-positive cancer. Therefore, the present disclosure provides methods of detecting P2RY8 in a sample. In various embodiments, the method

comprises contacting the sample with an antigen-binding protein, a conjugate, or a fusion protein, as described herein, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate or fusion protein bound to P2RY8 protein. The present disclosure also provides methods of diagnosing a P2RY8-positive cancer in a subject. In various embodiments, the method comprises contacting a biological sample comprising cells or tissue obtained from the subject with an antigen-binding protein, a conjugate, or a fusion protein, as described herein, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate or fusion protein bound to P2RY8 protein.

[00173] *Subjects*

[00174] In some embodiments of the present disclosure, the subject is a mammal, including, but not limited to, mammals of the order Rodentia, such as mice and hamsters, and mammals of the order Logomorpha, such as rabbits, mammals from the order Carnivora, including Felines (cats) and Canines (dogs), mammals from the order Artiodactyla, including Bovines (cows) and Swines (pigs) or of the order Perssodactyla, including Equines (horses). In some aspects, the mammals are of the order Primates, Ceboids, or Simoids (monkeys) or of the order Anthropoids (humans and apes). In some aspects, the mammal is a human.

[00175] *Kits*

[00176] In some embodiments, the antigen-binding proteins of the present disclosure are provided in a kit. In various aspects, the kit comprises the antigen-binding protein(s) as a unit dose. For purposes herein “unit dose" refers to a discrete amount dispersed in a suitable carrier. In various aspects, the unit dose is the amount sufficient to provide a subject with a desired effect, e.g., inhibition of cancer cell proliferation, inhibition of tumor growth, reduction of tumor size, treatment of cancer. Accordingly, provided herein are kits comprising an antigen-binding protein of the present disclosure optionally provided in unit doses. In various aspects, the kit comprises several unit doses, e.g., a week or month supply of unit doses, optionally, each of which is individually packaged or otherwise separated from other unit doses. In some embodiments, the components of the kit/unit dose are packaged with instructions for administration to a patient. In some embodiments, the kit comprises one or more devices for administration to a patient, e.g., a needle and syringe, and the like. In some aspects, the antigen-binding protein of the present disclosure, a pharmaceutically acceptable salt thereof, a conjugate comprising the antigen-binding protein, or a multimer or dimer comprising the antigen-binding protein, is pre-packaged in a

ready to use form, e.g., a syringe, an intravenous bag, etc. In some aspects, the kit further comprises other therapeutic or diagnostic agents or pharmaceutically acceptable carriers (e.g., solvents, buffers, diluents, etc.), including any of those described herein. In particular aspects, the kit comprises an antigen-binding protein of the present disclosure, along with an agent, e.g., a therapeutic agent, used in chemotherapy or radiation therapy.

[00177] *Various embodiments*

[00178] In various embodiments of the present disclosure, the antigen-binding protein binds to a human P2RY8 protein. In various embodiments of the present disclosure, merely by way of example, the antigen-binding protein binds to a crab-eating macaque (Macaca fascicularis) P2RY8 protein. For example, the antigen-binding protein binds to both a human P2RY8 protein and a crab-eating macaque (Macaca fascicularis) P2RY8 protein. For example, the antigen-binding protein binds to both a human P2RY8 protein and a crab-eating macaque (Macaca fascicularis) P2RY8 protein with about the same affinity within a 2-3 fold range. For example, the antigen-binding protein does not bind a dog P2RY8 protein or binds significantly less to a dog P2RY8 protein than a human P2RY8 protein. Merely by way of example, the antigen-binding protein binds a human P2RY8 protein with a binding affinity which is about 10x, 20x, 30x, 50x, 75x, 100x, 125x, 150x, 175x, 200x, 225x, 250x, 275x, 300x, or 325x greater than a binding affinity for a dog P2RY8 protein. In particular embodiments, the antigen-binding protein binds to both a human P2RY8 protein and a crab-eating macaque (Macaca fascicularis) P2RY8 protein, but does not bind or bind a dog P2RY8 protein with a binding affinity which is significantly less than that of a human P2RY8 protein by at least about 10x, 20x, 30x, 50x, 75x, 100x, 125x, 150x, 175x, 200x, 225x, 250x, 275x, 300x, or 325x.

[00179] In some embodiments, the antigen-binding protein comprises: (a) a heavy chain variable region amino acid sequence set forth in any one of Tables 2-3 and 14-31, or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a light chain variable region amino acid sequence set forth in the present disclosure, e.g., set forth in any one of Tables 2-3, and 14-31, or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (c) a combination comprising any one of (a) and any one of (b). In some embodiments, the variant sequence has at least about 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence

identity. In some embodiments, the antigen-binding protein of the present disclosure comprises a Fc polypeptide. In some embodiments, the antigen-binding protein of the present disclosure comprises a Fc polypeptide comprising an afucosylated glycan.

[00180] In some embodiments, the antigen-binding protein comprises (a) a heavy chain CDR1, (b) a heavy chain CDR2, (c) a heavy chain CDR3, (d) a light chain CDR1, (e) a light chain CDR2, (f) a light chain CDR3, or (g) a combination of any two or more of (a)-(f), wherein each CDR comprises the amino acid sequence are set forth in the present disclosure, e.g., set forth in any one of Tables 2-3 and 14-31, or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity.

[00181] In some embodiments, the antigen-binding protein comprises (a) a heavy chain FR1, (b) a heavy chain FR2, (c) a heavy chain FR3, (d) a heavy chain FR4, (e) a light chain FR1, (f) a light chain FR2, (g) a light chain FR3, (h) a light chain FR4, or (i) a combination of any two or more of (a)-(h), wherein each FR comprises the amino acid sequence are set forth in any one of Tables 2-3 and 14-31, or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity.

[00182] In some embodiments, the antigen-binding protein of the present disclosure is an antibody, e.g., a monoclonal antibody. In various aspects, the antibody is a chimeric antibody, a human antibody, or a humanized antibody. In various instances, the antigen-binding protein is an IgG. In various instances, the antigen-binding protein is a humanized IgG. In various instances, the antigen-binding protein is a human IgG. In various aspects, the antigen-binding protein inhibits at least about 50% colony growth of $P2RY8^+$ cancer cells in a soft agar 3D proliferation assay or inhibits tumor growth in xenograft mice injected with human $P2RY8^+$ cancer cells. In various aspects, the antigen-binding protein inhibits tumor growth in xenograft mice injected with $P2RY8^+$ cancer cells. In various instances, the antigen-binding protein inhibits at least 50% tumor growth in xenograft mice injected with $P2RY8^+$ cancer cells. In various aspects, tumor growth or cancer cell proliferation inhibition is observed with a "naked" fully formatted antibody (e.g., IgG1) wherein the "naked" fully formatted antibody comprises heavy and light chain variable and

constant regions and is free of a drug conjugate (e.g., not an antibody drug conjugate). In various aspects, the antigen-binding protein of the present disclosure induces antibody-dependent cell-mediated cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) activity.

[00183] The present invention includes a bispecific antigen-binding protein that binds P2RY8 protein and a second antigen, wherein the antigen-binding protein that binds P2RY8 is any one of the antigen-binding protein or a fragment thereof described herein. In some embodiments, the bispecific antigen-binding protein comprises: (a) a heavy chain variable region amino acid sequence set forth in any one of Tables 2-3 and 14-31, or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a light chain variable region amino acid sequence set forth in any one of Tables 2-3 and 14-31, or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (c) a combiination comprising any one of (a) and any one of (b). In some embodiments, the variant sequence has at least about 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% sequence identity. In some embodiments, the bispecific antigen-binding protein comprises a Fc polypeptide. In some embodiments, the bispecific antigen-binding protein comprises a Fc polypeptide comprising an afucosylated glycan.

[00184] In various aspects, a bispecific antigen-binding protein binds P2RY8 protein and a second antigen. In some embodiments, a bispecific antigen-binding protein comprises an antigen-binding fragment of an antibody specific for the second antigen. In various embodiments, the second antigen is a cell surface protein expressed by a T cell, optionally a component of the T-cell receptor (TCR), for example CD3. In some embodiments, the second antigen is CD3. In some embodiments, the second antigen is CD3E.

[00185] In various embodiments, the second antigen is a costimulatory molecule which assists in T-cell activation, e.g., CD40 or 4-1BB (CD137). In various embodiments, the second antigen is an Fc receptor, optionally, a Fc gamma receptor, Fc-alpha receptor, or Fc-epsilon receptor. In some embodiments, the Fc receptor is CD64 (Fc-gamma RI), CD32 (Fc-gamma RIIA), CD16A (Fc-gamma RIIIA), CD16b (Fc-gamma RIIIb), FcεRI, CD23 (Fc-epsilon RII), CD89 (Fc-epsilon RI), Fcα/μR, or FcRn. In some embodiments, the Fc receptor is CD16A.

[00186] In various embodiments, the second antigen is an immune checkpoint molecule, e.g., a protein involved in the immune checkpoint pathway, optionally, A2AR, B7-H3, B7-H4, BTLA, CTLA4, IDO, KIR, LAG3, NOX2, PD-1, TIM3, VISTA, or SIGLEC7. In some embodiments, the immune checkpoint molecule is PD-1, LAG3, TIM3, or CTLA4. In various embodiments, the bispecific antigen-binding protein comprises an scFv, a Fab, Fab', or a $F(ab')_2$ of any of the presently disclosed P2RY8 antibodies.

[00187] In various embodiments, the bispecific antigen-binding protein comprises an antigen-binding protein of the present disclosure. In various embodiments, the bispecific antigen-binding protein comprises a structure of a nanobody, a diabody, a BiTE®, DART, TandAb, CrossMab, or HSAbody.

[00188] The present disclosure provides a conjugate comprising an antigen-binding protein or a bispecific antigen-binding protein described herein and a heterologous moiety. In some embodiments, the conjugate comprises a cytotoxic agent or a chemotherapeutic agent. In some embodiments, the chemotherapeutic agent is an anti-mitotic agent which inhibits cell division by blocking tubulin polymerization. In some embodiments, the anti-mitotic agent is an auristatin. In some embodiments, the auristatin is MMAE.

[00189] In various embodiments, the conjugate of the present disclosure is conjugated to the antigen-binding protein via a cleavable linker. In some embodiments, the cleavable linker is VC-PAB.

[00190] In some embodiments, the conjugate comprises an antigen-binding protein that is an antibody. The antibody is a monoclonal antibody, optionally wherein the monoclonal antibody is an IgG antibody. In some embodiments, the antibody is a human antibody, humanized antibody, or a chimeric antibody.

[00191] In various embodiments, the conjugate of the present disclosure has an average number of units of the agent conjugated per antigen-binding protein in a range of 1 to 8, preferably wherein the average number of units of the agent conjugated per antigen-binding protein is in a range of 3-8. In some embodiments, the conjugate is a heterogeneous conjugate. In other embodiments, the conjugate is a homogeneous conjugate. In some embodiments, the conjugate comprises a heterologous moiety or an agent, wherein the agent is conjugated at a specific site of the antigen-binding protein. In some embodiments, the specific site is an unpaired cysteine residue. In some embodiments, the unpaired cysteine residue may be obtained from reduction of a disulfide bond. In some embodiments, the unpaired cysteine residue may be obtained from reduction of an interchain disulfide

bond in the hinge region of an antibody. In some embodiments, the antibody with the reduced interchain disulfide bond in the hinge region is an IgG isotype. In some embodiments, the IgG isotype is IgG1 or IgG2. In some embodiments, the IgG isotype is humanized. In some embodiments, the IgG isotype is humanized IgG1. In some embodiments, the conjugate comprises a humanized IgG and a heterologous moiety or an agent. In some embodiments, the conjugate comprises a humanized IgG1 or humanized IgG2 and a heterologous moiety or an agent. In some embodiments, the conjugate comprises a humanized IgG1 and a heterologous moiety or an agent. In some embodiments, the conjugate comprises a humanized IgG1 or humanized IgG2 and 3-8 units of heterologous moiety or agent. In some embodiments, the average number of the heterologous moiety or agent is in the range of about 3-8 units per humanized IgG1 or humanized IgG2. In some embodiments, the conjugate comprises a humanized IgG1 and 4 units of heterologous moiety or agent. In some embodiments, the average number of the heterologous moiety or agent is in the range of about 4 units per humanized IgG. In preferred embodiments, the homogeneous conjugates comprise the HAR of 4. In other preferred embodiments, the homogeneous conjugates comprise the HAR of 2. In some embodiments, the homogeneous conjugates comprise greater than or equal to 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 percent conjugates with the defined HAR. In some embodiments, the homogeneous conjugates comprise about 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 percent conjugates with the defined HAR. In some embodiments, the homogeneous conjugates comprise at least 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, or 100 percent conjugates with the defined HAR. In some embodiments, the homogeneous conjugates comprise the HAR distribution that is not Gaussian or quasi-Gaussian distribution. In some embodiments, the homogeneity of the homogeneous conjugates is determined by a chromatogram, *e.g.*, HPLC or any suitable chromatography. In some embodiments, the chromatogram is a HIC chromatogram. The homogeneous conjugate may be generated by a site-specific conjugation.

[00192] In some embodiments, an antigen-binding protein, a bispecific antigen-binding protein, or a conjugate may be detectably labeled. Examples of detectable moieties include various enzymes, prosthetic groups, fluorescent materials, luminescent materials, bioluminescent materials, and radioactive materials. Examples of suitable enzymes include

horseradish peroxidase, alkaline phosphatase, β-galactosidase, luciferase, or acetylcholinesterase; examples of suitable prosthetic group complexes include streptavidin/biotin and avidin/biotin; examples of suitable fluorescent materials include umbelliferone, fluorescein, fluorescein isothiocyanate (FITC), rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin (PE); an example of a luminescent material includes luminol; examples of bioluminescent materials include luciferase, luciferin, and aequorin, and examples of suitable radioactive material include ^{125}I, ^{131}I, ^{35}S, or ^{3}H. As used herein, the term "labeled", with regard to the antigen-binding protein, bispecific antigen-binding protein, or conjugate is intended to encompass direct labeling by coupling (*i.e.*, physically linking) a detectable substance, such as a radioactive agent or a fluorophore (*e.g.* fluorescein isothiocyanate (FITC) or phycoerythrin (PE) or indocyanine (Cy5)) to the protein or conjugate, as well as indirect labeling of the antibody by reactivity with a detectable substance. For example, an antigen-binding protein, a bispecific antigen-binding protein, or a conjugate may be labeled with a nucleic acid sequence that may be amplified and detected, or an antisense oligonucleotide to reduce expression of a particular gene, such that expression can then be detected and measured. In some embodiments, an antigen-binding protein, a bispecific antigen-binding protein, or a conjugate may be detectably labeled by comprising a peptide (HA, myc, GST, etc.) or a polypeptide (GFP or the like) as a fusion protein.

[00193] The present disclosure also provides a fusion protein comprising an antigen-binding protein or a bispecific antigen-binding protein described herein. The present disclosure further provides a nucleic acid comprising a nucleotide sequence encoding an antigen-binding protein, a bispecific antigen-binding protein, a conjugate, or a fusion protein, of the present disclosure. In various aspects, the conjugate may be a fusion protein of an antigen-binding protein and a second protein or peptide. The present disclosure provides a vector comprising the nucleic acid comprising a nucleotide sequence encoding an antigen binding protein, a conjugate, or a fusion protein, of the present disclosure. The present disclosure additionally provides a host cell comprising the nucleic acid or the vector of the present disclosure.

[00194] The present disclosure provides a method of producing an antigen-binding protein or a bispecific antigen-binding protein that binds to a P2RY8 protein, comprising (i) culturing the host cell of the present disclosure in a cell culture medium, wherein the host cell comprises a nucleic acid comprising a nucleotide sequence encoding an antigen binding

protein or a bispecific antigen-binding protein described herein, and (ii) harvesting the antigen-binding protein or a bispecific antigen-binding protein from the cell culture medium. Also, provided is a method of producing a fusion protein comprising an antigen-binding protein or a bispecific antigen-binding protein that binds to a P2RY8 protein, comprising (i) culturing the host cell of the present disclosure in a cell culture medium, wherein the host cell comprises a nucleic acid comprising a nucleotide sequence encoding a fusion protein of the present disclosure, and (ii) harvesting the fusion protein from the cell culture medium.

[00195] The present disclosure furthermore provides a method of producing a pharmaceutical composition comprising combining an antigen-binding protein of the invention, a bispecific antigen-binding protein, a conjugate, a fusion protein, a nucleic acid, a vector, a host cell, of the present disclosure, or a combination thereof, and a pharmaceutically acceptable carrier, diluent or excipient. Also provided are pharmaceutical compositions comprising antigen-binding protein, a bispecific antigen-binding protein, a conjugate, a fusion protein, a nucleic acid, a vector, a host cell, of the present disclosure, or a combination thereof, and a pharmaceutically acceptable carrier, diluent or excipient.

[00196] Provided herein is a method of treating a subject with a P2RY8-expressing cancer comprising administering to the subject a pharmaceutical composition described herein in an amount effective to treat the cancer. Also provided is a method of inhibiting tumor growth in a subject, comprising administering to the subject a pharmaceutical composition described herein in an amount effective to inhibit tumor growth, wherein the tumor expresses P2RY8. The present disclosure provides a method of reducing tumor size in a subject, comprising administering to the subject a pharmaceutical composition described herein in an amount effective to reduce tumor size, wherein the tumor expresses P2RY8. Further provided is a method of preventing the recurrence of cancer in a subject, comprising administering to the subject a pharmaceutical composition described herein in an amount effective to prevent the recurrence of cancer, wherein the tumor expresses P2RY8.

[00197] The present disclosure provides a method of detecting P2RY8 protein in a sample, comprising contacting the sample with an antigen-binding protein of the invention, a bispecific antigen-binding protein, a conjugate, or a fusion protein, of the present disclosure, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate or fusion protein bound to P2RY8 protein. Also provided herein is a method of

diagnosing a P2RY8-positive cancer in a subject, comprising contacting a biological sample comprising cells or tissue obtained from the subject with an antigen-binding protein, a bispecific antigen-binding protein, a conjugate, or a fusion protein, of the present disclosure, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate or fusion protein bound to P2RY8 protein.

[00198] Additional exemplary embodiments are presented below.

1. An antigen-binding protein comprising: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 177) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

2. The antigen-binding protein embodiment 1 comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 178) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 179) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 180) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 186) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 187) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO:

188) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

3. An antigen-binding protein comprising: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

4. An antigen-binding protein comprising (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 161) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 169) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

5. An antigen-binding protein comprising: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity;

and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 201) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

6. An antigen-binding protein comprising: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

7. An antigen-binding protein comprising: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 233) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

8. An antigen-binding protein comprising: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI

TYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

9. An antigen-binding protein comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 146) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 147) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 148) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 154) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 155) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 156) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

10. An antigen-binding protein comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 162) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 163) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO:

164) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 170) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 171) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 172) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

11. An antigen-binding protein comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 194) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 195) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 196) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 202) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 203) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 204) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

12. An antigen-binding protein comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 210) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 211) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy

chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 212) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 218) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 219) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 220) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

13. An antigen-binding protein comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 226) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 227) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 228) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO:234) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 235) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 236) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

14. An antigen-binding protein comprising: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 242) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 243) or a variant sequence thereof which differs by only one

or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 244) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 250) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 251) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 252) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

15. The antigen-binding protein of embodiment 9, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 149) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 150) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 151) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 152) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 157) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 158) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO:

159) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 comprising the amino acid sequence: FGQGTKLEIK (SEQ ID NO: 160) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or more of (a)-(h).

16. The antigen-binding protein of embodiment 10, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 165) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 166) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 167) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 168) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 173) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 174) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 175) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 comprising the amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 176) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or more of (a)-(h).

17. The antigen-binding protein of embodiment 2, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 181) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 182) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 183) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 184) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 189) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 190) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 191) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 192) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

18. The antigen-binding protein of embodiment 11, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 197) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 198) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about

85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 199) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 200) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 205) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 206) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 207) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 208) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

19. The antigen-binding protein of embodiment 12, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 213) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 214) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 215) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 216) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the

amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 221) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 222) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYC (SEQ ID NO: 223) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 224) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

20. The antigen-binding protein of embodiment 13, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 229) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 230) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 231) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 232) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 237) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 238) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC (SEQ ID NO:

239) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 240) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

21. The antigen-binding protein of embodiment 14, additionally comprising: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 245) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 246) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 247) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 248) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 253) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 254) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 255) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 256) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

22. An antigen-binding protein comprising: (a) a heavy chain variable region having the amino acid sequence of:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

23. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 161) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 169) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

24. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 177) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL

EIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

25. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 201) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

26. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

27. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 233) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

28. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

29. The antigen-binding protein of any one of the previous embodiments, wherein the variant sequence has at least about 80% or at least or about 85% sequence identity.

30. The antigen-binding protein of any one of the previous embodiments, wherein the variant sequence has at least about 90% sequence identity or at least or about 95% sequence identity.

31. The antigen-binding protein of embodiment of any one of the previous embodiments, wherein:

(a) the antigen-binding protein binds to a human P2Y receptor family member 8 (P2RY8) protein (SEQ ID NO: 369); (b) the antigen-binding protein binds an extracellular domain of human P2RY8 with a dissociation constant (K_D) of about less than 10 nM, 5 nM, 2.5 nM, 1 nM, 0.5 nM or 0.25 nM; (c) the antigen-binding protein preferentially binds human P2RY8 over dog P2RY8 (SEQ ID NO: 371); (d) the antigen-binding protein does not bind dog P2RY8; or (e) any combination thereof.

32. The antigen-binding protein of embodiment 31, wherein the human P2RY8 (SEQ ID NO: 369) is expressed on the surface of a cell; the dog P2RY8 (SEQ ID NO: 371) is expressed on the surface of a cell; and the antigen-binding protein preferentially

binds the human P2RY8 over dog P2RY8 by a factor of at least about 10x, 20x, 30x, 50x, 75x, 100x, 125x, 150x, 175x, 200x, 225x, 250x, 275x, 300x, or 325x.

33. The antigen-binding protein of any one of the previous embodiments, which is an antibody or antigen-binding antibody fragment.

34. The antigen-binding protein of embodiment 33, wherein the antibody is a monoclonal antibody.

35. The antigen-binding protein of embodiment 33 or 34, wherein the antibody is a human or humanized antibody.

36. The antigen-binding protein of any one of embodiments 33-35, which is an IgG.

37. The antigen-binding protein of embodiment 36, wherein the IgG is selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.

38. The antigen-binding protein of embodiment 36 or 37, wherein the IgG is IgG1.

39. The antigen-binding protein of embodiment 33, wherein the antigen-binding antibody fragment is selected from the group consisting of scFv, $F(ab')_2$, Fab, Fab', and Fv.

40. The antigen-binding protein of any one of the previous embodiments, which inhibits tumor growth in xenograft mice injected with human cancer cells.

41. The antigen-binding protein of any one of the previous embodiments, wherein the antigen-binding protein comprises (a) an Fc polypeptide, or (b) an Fc polypeptide comprising an afucosylated glycan.

42. A conjugate comprising an antigen-binding protein of any one of the previous embodiments or those described herein, or an antigen-binding fragment thereof.

43. The conjugate of embodiment 42 comprising a cytotoxic agent or a chemotherapeutic agent.

44. The conjugate of embodiment 43, wherein the chemotherapeutic agent is an anti-mitotic agent which inhibits cell division by blocking tubulin polymerization.

45. The conjugate of embodiment 44, wherein the anti-mitotic agent is an auristatin.

46. The conjugate of embodiment 45, wherein the auristatin is monomethyl auristatin E (MMAE).

47. The conjugate of any one of embodiments 43-46, wherein the agent is conjugated to the antigen-binding protein via a cleavable linker.

48. The conjugate of embodiment 47, wherein the cleavable linker is VC-PAB.

49. The conjugate of any one of embodiments 42-48, wherein the antigen-binding protein is an antibody.

50. The conjugate of embodiment 49, wherein the antibody is a monoclonal antibody.

51. The conjugate of embodiment 49 or 50, wherein the antibody is a human antibody, humanized antibody, or a chimeric antibody.

52. The conjugate of any one of embodiments 49-51, wherein the antibody is an IgG antibody, optionally wherein the IgG is IgG1.

53. The conjugate of any one of embodiments 42-52, wherein an average number of units of an agent conjugated per antigen-binding protein is in a range of 1 to 8, preferably wherein the average number of units of an agent conjugated per antigen-binding protein is in a range of 3-8.

54. The conjugate of any one of embodiments 42-53, wherein the conjugate is a heterogeneous conjugate.

55. The conjugate of any one of embodiments 42-53, wherein the conjugate is a homogeneous conjugate.

56. The conjugate of any one of embodiments 42-55, wherein an agent is conjugated at a specific site of the antigen-binding protein.

57. The conjugate of embodiment 56, wherein the specific site is an unpaired cysteine residue.

58. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 145 and SEQ ID NO: 153 conjugated to VC-PAB-MMAE.

59. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 161 and SEQ ID NO: 169 conjugated to VC-PAB-MMAE.

60. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 177 and SEQ ID NO: 185 conjugated to VC-PAB-MMAE.

61. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 193 and SEQ ID NO: 201 conjugated to VC-PAB-MMAE.

62. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 209 and SEQ ID NO: 217 conjugated to VC-PAB-MMAE.

63. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 225 and SEQ ID NO: 233 conjugated to VC-PAB-MMAE.

64. The conjugate of any one of embodiments 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 241 and SEQ ID NO: 249 conjugated to VC-PAB-MMAE.

65. A bispecific antigen-binding protein comprising the antigen-binding protein of any one of embodiments 1-41, an antigen binding protein of Table 3, or a fragment thereof that binds to a human P2Y receptor family member 8 (P2RY8) protein (SEQ ID NO: 369) and a second antigen-binding protein that binds a second antigen.

66. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 177) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

67. The bispecific antigen-binding protein of embodiment 66, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 178) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 179) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 180) or a variant sequence thereof which differs by only one or two amino

acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 186) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 187) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 188) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

68. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

69. The bispecific antigen-binding protein of embodiment 68, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 146) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 147) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 148) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1

comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 154) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 155) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 156) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

70. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 161) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 169) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

71. The bispecific antigen-binding protein of embodiment 70, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 162) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 163) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 164) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 170) or a

variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 171) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 172) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

72. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 201) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

73. The bispecific antigen-binding protein of embodiment 72, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 194) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 195) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 196) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 202) or a variant sequence thereof which differs by only one or two amino acids or which has at

least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 203) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 204) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

74. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

75. The bispecific antigen-binding protein of embodiment 74, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 210) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 211) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 212) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 218) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid

sequence of: RAS (SEQ ID NO: 219) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 220) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

76. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 233) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

77. The bispecific antigen-binding protein of embodiment 76, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 226) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 227) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 228) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO:234) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 235) or a variant sequence thereof which differs by

only one or two amino acids or which has at least or about 70% sequence identity; (f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 236) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

78. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

79. The bispecific antigen-binding protein of embodiment 78, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 242) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 243) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 244) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 250) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 251) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; (f) a

light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 252) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or (g) a combination of any two or moreof (a)-(f).

80. The bispecific antigen-binding protein of embodiment 66, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 181) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 182) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 183) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 184) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 189) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 190) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 191) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 192) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or more of (a)-(h).

81. The bispecific antigen-binding protein of embodiment 68, wherein the antigen-

binding protein that binds to the P2RY8 protein additionally comprises: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 149) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 150) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 151) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 152) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 157) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 158) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 159) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 comprising the amino acid sequence: FGQGTKLEIK (SEQ ID NO: 160) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

82. The bispecific antigen-binding protein of embodiment 70, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 165) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid

sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 166) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 167) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 168) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 173) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 174) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 175) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 comprising the amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 176) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or more of (a)-(h).

83. The bispecific antigen-binding protein of embodiment 72, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 197) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 198) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 199) or a variant sequence thereof which differs by only one or two amino acids or

which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 200) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 205) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 206) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 207) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 208) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

84. The bispecific antigen-binding protein of embodiment 74, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 213) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 214) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 215) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 216) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 221) or a variant sequence thereof which differs by only one or two amino acids or which has at

least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 222) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYC (SEQ ID NO: 223) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 224) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

85. The bispecific antigen-binding protein of embodiment 76, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 229) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 230) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 231) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 232) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 237) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 238) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC (SEQ ID NO: 239) or a variant sequence thereof which differs by only one or two amino acids or

which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 240) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

86. The bispecific antigen-binding protein of embodiment 78, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises: (a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 245) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 246) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (c) a heavy chain FR3 comprising the amino acid sequence: TYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 247) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 248) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 253) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 254) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 255) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; (h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 256) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or (i) a combination of any two or moreof (a)-(h).

87. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable

region having the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI
TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV
WGQGTTVTVSS (SEQ ID NO: 177) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or (b) a light chain variable region having the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY
RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL
EIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

88. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable region having the amino acid sequence of:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT
YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV
WGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or (b) a light chain variable region having the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY
RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL
EIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

89. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable region having the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWVSYIT
YSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCARGYWYFDV
WGQGTTVTVSS (SEQ ID NO: 161) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or
(b) a light chain variable region having the amino acid sequence:

DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 169) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

90. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 201) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

91. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

92. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable region having the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYR ASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEI K (SEQ ID NO: 233) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

93. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises: (a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDV WGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

94. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein is selected from the group consisting of: (a) an antigen-binding protein comprising: (i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 257) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKPGKAPKLLIY RASNVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDLLTFGQGTK LEIK (SEQ ID NO: 265) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; (b) an antigen-binding protein comprising: (i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 273) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGKAPKLLIYR ASNVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDLLTFGQGTKLE IK (SEQ ID NO: 281) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; (c) an antigen-binding protein comprising: (i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 289) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKPGKAPKLLIY RASNVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDLLTFGQGTK LEIK (SEQ ID NO: 297) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and (d) an antigen-binding protein comprising: (i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 305) or a variant sequence thereof which differs by

only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGKAPKLLIYR ASNVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDLLTFGQGTKLE IK (SEQ ID NO: 313) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

95. The bispecific antigen-binding protein of embodiment 65, wherein the antigen-binding protein that binds to the P2RY8 protein is selected from the group consisting of: (a) an antigen-binding protein comprising: (i) a heavy chain variable region having the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 257) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or (ii) a light chain variable region having the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKPGKAPKLLIY RASNVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDLLTFGQGTK LEIK (SEQ ID NO: 265) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; (b) an antigen-binding protein comprising: (i) a heavy chain variable region having the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 273) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) a light chain variable region having the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGKAPKLLIYR ASNVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDLLTFGQGTKLE IK (SEQ ID NO: 281) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; (c) an antigen-binding protein comprising:

(i) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 289) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKPGKAPKLLIY RASNVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDLLTFGQGTK LEIK (SEQ ID NO: 297) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and (d) an antigen-binding protein comprising: (i) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYI TYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDV WGQGTTVTVSS (SEQ ID NO: 305) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or (ii) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGKAPKLLIYR ASNVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDLLTFGQGTKLE IK (SEQ ID NO: 313) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

96. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is a cell surface protein expressed by a T-cell, optionally, a component of the T-cell receptor (TCR), for example, CD3.

97. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is a costimulatory molecule which assists in T-cell activation, e.g., CD40 or 4-lBB (CD137).

98. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is an Fc receptor, optionally, a Fc gamma receptor, Fc-alpha receptor, or Fc-epsilon receptor.

99. The bispecific antigen-binding protein of embodiment 98, wherein the Fc receptor is CD64 (Fc-gamma RI), CD32 (Fc-gamma RIIA), CD16A (Fc-gamma RIIIA), CD16b (Fc-gamma RIIIb), FcεRI, CD23 (Fc-epsilon RII), CD89 (Fc-epsilon

RI), Fcα/μR, or FcRn.

100. The bispecific antigen-binding protein of embodiment 98 or 99, wherein the Fc receptor is CD16A.

101. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is an immune checkpoint molecule, e.g., a protein involved in the immune checkpoint pathway, optionally, A2AR, B7-H3, B7-H4, BTLA, CTLA4, IDO, KIR, LAG3, NOX2, PD-1, TIM3, VISTA, or SIGLEC7.

102. The bispecific antigen-binding protein of embodiment 101, wherein the immune checkpoint molecule is PD-1, LAG3, TIM3, or CTLA4.

103. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is CD3.

104. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is CD3E.

105. The bispecific antigen-binding protein of any one of embodiments 65-95, wherein the second antigen is CD16A.

106. The bispecific antigen-binding protein of any one of embodiments 65-105, comprising an scFv, a Fab, or a $F(ab')_2$ of any of the presently disclosed P2RY8 antibodies.

107. The bispecific antigen-binding protein of any one of embodiments 65-106, comprising a structure of a nanobody, BiTE®, DART, TandAb, CrossMab, or HSAbody.

108. A fusion protein comprising an antigen-binding protein of any one of the previous embodiments or those described herein, or an antigen-binding fragment thereof.

109. A nucleic acid comprising a nucleotide sequence encoding the antigen binding protein of any one of embodiments 1-41, the bispecific antigen-binding protein of any one of embodiments 65-107, or the fusion protein of embodiment 108.

110. The nucleic acid of embodiment 109, wherein the nucleic acid is a complementary DNA (cDNA).

111. A vector comprising the nucleic acid of embodiment 109 or 110.

112. The vector of embodiment 111, additionally comprising an internal ribosome entry site (IRES).

113. A host cell comprising the nucleic acid of embodiment 109, the cDNA of

embodiment 110, or the vector of embodiment 111 or 112.

114. The host cell of embodiment 113, wherein the host cell is a bacterial cell.

115. The host cell of embodiment 113, wherein the host cell is a eukaryotic cell.

116. The host cell of embodiment 113 or 115, wherein the host cell is a mammalian cell.

117. The host cell of embodiment 116, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.

118. A method of producing an antigen-binding protein that binds to a P2Y receptor family member 8 (P2RY8) protein, comprising (i) culturing the host cell of any one of embodiments 113-117 in a cell culture medium, and (ii) harvesting the antigen-binding protein from the cell culture medium.

119. A method of producing a bispecific antigen-binding protein comprising an antigen-binding protein that binds to a P2Y receptor family member 8 (P2RY8) protein, comprising (i) culturing the host cell of any one of embodiments 113-117 in a cell culture medium, and (ii) harvesting the bispecific antigen-binding protein from the cell culture medium.

120. A method of producing a fusion protein comprising an antigen-binding protein that binds to a P2Y receptor family member 8 (P2RY8) protein, comprising (i) culturing the host cell of any one of embodiments 113-117 in a cell culture medium, and (ii) harvesting the fusion protein from the cell culture medium.

121. A method of producing a pharmaceutical composition comprising combining the antigen-binding protein of any one of embodiments 1-41, the conjugate of any one of embodiments 42-64, the bispecific antigen-binding protein of any one of embodiments 65-107, the fusion protein of embodiment 108, the nucleic acid of embodiment 109 or 110, the vector of embodiment 111 or 112, the host cell of any one of embodiments 113-117, or a combination thereof; and a pharmaceutically acceptable carrier, diluent, or excipient.

122. A pharmaceutical composition comprising the antigen-binding protein of any one of embodiments 1-41, the conjugate of any one of embodiments 42-64, the bispecific antigen-binding protein of any one of embodiments 65-107, the fusion protein of embodiment 108, the nucleic acid of embodiment 109 or 110, the vector of embodiment 111 or 112, the host cell of embodiment any one of embodiments 113-117, or a combination thereof; and a pharmaceutically acceptable carrier, diluent, or excipient.

123. A method of treating a subject with a P2RY8-expressing cancer comprising administering to the subject the pharmaceutical composition of embodiment 122 in an amount effective to treat the cancer.

124. A method of inhibiting tumor growth in a subject, comprising administering to the subject the pharmaceutical composition of embodiment 122 in an amount effective to inhibit tumor growth.

125. A method of reducing tumor size in a subject, comprising administering to the subject the pharmaceutical composition of embodiment 122 in an amount effective to reduce tumor size.

126. A method of preventing the recurrence of cancer in a subject, comprising administering to the subject the pharmaceutical composition of embodiment 122 in an amount effective to prevent the recurrence of cancer.

127. The method of any one of embodiments123-126, wherein the pharmaceutical composition induces apoptosis in tumor cells.

128. The method of any one of embodiments 123-126, wherein the pharmaceutical composition induces apoptosis in cells expressing P2RY8.

129. A method of detecting the P2Y receptor family member 8 (P2RY8) protein or a fragment thereof in a sample, comprising contacting the sample with the antigen-binding protein of any one of embodiments 1-41, the conjugate of any one of embodiments 42-64, the bispecific antigen-binding protein of any one of embodiments 65-107, or the fusion protein of embodiment 108, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate, or fusion protein bound to the P2RY8 protein or a fragment thereof.

130. A method of diagnosing a P2Y receptor family member 8 (P2RY8) protein-positive cancer in a subject, comprising contacting a sample (e.g., biological sample comprising cells or tissue) from the subject with the antigen-binding protein of any one of embodiments 1-41, the conjugate of any one of embodiments 42-64, the bispecific antigen-binding protein of any one of embodiments 65-107, or the fusion protein of embodiment 108, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate, or fusion protein bound to the P2RY8 protein or a fragment thereof.

[00199] The following examples are given merely to illustrate the present disclosure and not in any way to limit its scope.

EXAMPLES

EXAMPLE 1: P2RY8 RNA EXPRESSION IN NORMAL HUMAN TISSUES AND CELLS, HUMAN TUMORS AND HUMAN CANCER CELL LINES

[00200] This example demonstrates an analysis of P2RY8 RNA levels in normal human tissues, primary human cancers and human cancer cell line panel the Translational Oncology Research laboratory (TORL) from human cancer patients.

[00201] P2RY8 RNA expression in normal human tissues as provided in GTEx database, GTEx_Analysis_2017-06-05_v8_RNASeQCv1.1.9_gene_tpm, is downloaded from GTEx portal (World Wide Web at gtexportal.org/home/datasets) and presented as a box plot (**Fig. 1**). The Cancer Genome Atlas (TCGA) database managed by the National Cancer Institute (NCI) is used to download P2RY8 RNA expression data from a total of 10,071 human cancer tissue samples through cBioPortal (World Wide Web at cbioportal.org/) and plotted with ggplot2 package in R programing language. **Fig. 2** is a box plot of P2RY8 expression in human cancer from TCGA, showing high levels of P2RY8 RNA expression in a number of human cancers, particularly mature B-cell neoplasms and leukemia.

[00202] P2RY8 expression levels were measured in a panel of human cancer cell lines curated by TORL using Agilent 44K microarrays (4x44K array chip, Agilent Technologies, Santa Clara, CA) and RNA sequencing (RNA-Seq) assays. RNASeq was performed by BGI Americas (Cambridge, MA) using its "RNASeq for quantification" service. A total of 587 human cancer cell lines were analyzed for P2RY8 RNA expression. As shown in **Fig. 3**, human cancer cell lines derived from acute myeloid leukemia (AML), lymphoma, and myeloma (e.g., multiple myeloma) cancer patients expressed the highest levels of P2RY8; whereas, cancer cell lines derived from sarcoma and cancers of the connective tissue, prostate, lung, melanoma, colon, endometrium, pancreas, ovary, kidney, liver, breast, upper GI, head-and-neck, and bladder generally showed low P2RY8 RNA expression.

EXAMPLE 2: PRODUCTION OF CELLS ENGINEERED TO OVEREXPRESS P2RY8

[00203] This example demonstrates the production of cells engineered to overexpress P2RY8.

[00204] Models engineered to overexpress P2RY8 were generated. Briefly, a nucleotide sequence encoding P2RY8 protein was introduced into a lentiviral vector having a CMV promoter and an internal ribosome entry site (IRES) of encephalomyocarditis virus (EMCV). The IRES was located between the Gene of Interest (GOI) cDNA (P2RY8) and

puromycin cDNA. A woodchuck posttranscriptional regulatory element (WPRE) was located downstream of the puromycin cDNA. The vector also expressed either a GFP marker sequence or a MycDDK epitope tag, optionally, as a fusion protein comprising P2RY8 protein and GFP marker or MycDDK epitope tag.

[00205] The expression vector was virally transduced into HEK293T cells (for screening purposes) and NIH3T3 cells (for immunizations). Positively transduced cells were selected based on survival in medium containing puromycin (1 μg/ml). The positive cells were subcloned to obtain a stable, uniform, clonal population of P2RY8 overexpressing cells.

[00206] Subcloned P2RY8-overexpressing cells were confirmed by fluorescence microscopy using a GFP tag to confirm overexpression of P2RY8 protein.

[00207] Further, cell surface expression of P2RY8 protein was confirmed by flow cytometry using a P2RY8 monoclonal antibody (mAb) (Abcam, Waltham, MA; catalog #: ab169392) on a BD Biosciences Accuri™ flow cytometer (San Jose, CA) and an Alexa Fluor® 647 goat anti-mouse IgG (minimal x-reactivity) secondary antibody (Biolegend, San Diego, CA; Catalog #: 405322). Briefly, the P2RY8-expressing cells were incubated with anti-P2RY8 antibody for 30 min on ice, and after washing, incubated with AF647 goat anti-mouse IgG antibody for 30 min one ice. Fluorescence was read by a BD Biosciences Accuri™ flow cytometer (San Jose, CA). In addition to the monoclonal antibody, a polyclonal P2RY8 antibody (Abnova, Taipei, Taiwan; catalog #: PAB16354) was also used in the characterization of the P2RY8-expressing cells.

[00208] In addition to producing stable cell lines with cell surface expression of human P2RY8 protein (UniProt accession number: Q86VZ1; Table 9, SEQ ID NO: 369; see **Fig. 4 and Table 38**) in HEK293T cells and NIH3T3 cells, P2RY8 from crab-eating macaque (*Macaca fascicularis*; NCBI RefSeq accession number: XP_005595888; Table 9, SEQ ID NO: 370; see **Fig. 4 and Table 38**) and dog (NCBI RefSeq accession number: XP_013967130; Table 9, SEQ ID NO: 371; see **Fig. 4 and Table 38**) were expressed as fusion proteins to mGFP marker (see **Table 39**) by transient transfection in HEK293T cells to characterize species selectivity of anti-P2RY8 antibody binding. **Fig. 4** is a sequence alignment of human, crab-eating macaque and dog P2RY8 proteins.

EXAMPLE 3: PRODUCTION OF P2RY8-SPECIFIC ANTIBODIES

[00209] P2RY8-specific antibodies were produced by immunizing Balb/c, CD1, and an F1 cross of Balb/c with C57BL/6 mice with NIH3T3 stable cells overexpressing full length

human P2RY8 protein (UniProt accession number: Q86VZ1; SEQ ID NO: 369). The human P2RY8-expressing NIH3T3 stable cells were obtained following viral transduction of a mammalian expression vector encoding a human P2RY8-myc-DDK fusion protein into NIH3T3 cells.

[00210] Splenocytes were harvested from the immunized mice and fused with myeloma lines by BTX Electrofusion (BTX, Holliston, MA) to generate hybridomas. 7000 primary hybridoma cultures were generated and cultured in 384-well plates. The ability of the antibodies to bind peptides and/or human cancer cells that expressed P2RY8 protein was assessed by flow cytometry. Potential positive antibodies were re-arrayed into 96 well plates and further screened by flow cytometry against endogenous and artificial cell line models that have sequence similarity to the human P2RY8 protein (e.g., artificial cell line models that express monkey or dog P2RY8 protein).

[00211] Hybridomas positive for producing antibodies that bind human P2RY8 protein, but preferably not dog P2RY8 protein, were identified, and nucleic acid sequences encoding immunoglobulin light and heavy chain directed against human P2RY8 protein were isolated. These nucleic acid sequences were used to produce P2RY8 antibodies formatted as full-length IgG antibodies (e.g., chimeric or humanized IgG1) using ExpiCHO™ Expression System (ThermoFisher Scientific, Waltham, MA; catalog #: A29133). The heavy and light chain variable regions of the antibodies were cloned into an antibody expression vector which was engineered in the lab based on a pcDNA™3.4-TOPO® vector (ThermoFisher Scientific, Waltham, MA; catalog #: A14697). Transfection of the antibody expression vector into CHO cells, according to protocol provided in the ExpiCHO™ Expression System kit resulted in production of a bicistronic mRNA in which both immunoglobulin heavy and light chains were obtained from the bicistronic mRNA, and an IRES drove the expression of the second immunoglobulin chain. The produced antibodies were purified using protein A resins and/or size exclusion.

[00212] Cell surface binding of the antibodies to P2RY8 protein and the antibody IC50 were determined by FACS in which P2RY8 antibodies were directly conjugated with Alexa Fluor® 647 NHS Ester (Succinimidyl Ester) (ThermoFisher Scientific, Waltham, MA; catalog #: A20106) following the manufacturer's protocol. Alternatively, the purified P2RY8 antibodies were used in an indirect immunofluorescence assay using Alexa Fluor® 647 goat anti-mouse IgG (minimal x-reactivity) secondary antibody (Biolegend, San Diego, CA; catalog #: 405322).

[00213] P2RY8-expressing cells were used in FACS assays to determine the P2RY8 antibody's ability to bind to P2RY8 protein on the surface of cells. HEK293T cells engineered to express human P2RY8 fused to GFP, crab-eating macaque P2RY8 fused to GFP, or dog P2RY8 fused to GFP were used as artificial models of P2RY8 expression (Tables 13 and 39). SU-DHL-5 (ATCC CRL-2958), SU-DHL-10, (ATCC CRL-2963), and Karpas-1106P (RRID: CVCL_1821) cells were used as endogenous models of P2RY8 expression.

[00214] For each type of cell tested and for each mAb, suspension cells were used without a need to treat with Versene®, whereas adherent cells were detached from the surface of the culture flasks by Versene® (instead of trypsin) in order to protect the cell surface proteins. The cells were collected, washed, resuspended and then incubated with Alexa Fluor®-labeled P2RY8 mAbs for 30 min in the dark on ice at a pre-determined concentration. The P2RY8 mAbs were directly labeled with Alexa Fluor® 647 NHS Ester (Succinimidyl Ester). Alternatively, unlabeled P2RY8 antibodies may be detected using a fluorescently labeled secondary antibody. After washing, the cells were read by a BD Accuri™ Flow Cytometer C6 to detect antibody-antigen protein binding in the FL4-H channel.

EXAMPLE 4: CHARACTERIZATION OF CHIMERIC MOUSE IgG mABS

[00215] Chimeric P2RY8 antibodies comprising the heavy and light chain variable region and human constant IgG1-kappa or lambda constant region in place of mouse constant region were analyzed for ability to inhibit tumor growth or reduce tumor size grow in xenograft models of human tumors.

[00216] *In vivo* binding studies were carried out in xenograft mice injected with human cancer cell lines. Briefly, xenograft models of human cancer cell lines were established in six-week-old SCID mice (Charles River Laboratories). The following conditions were followed for subcutaneous injection of each cell line: SU-DHL-5 (ATCC CRL-2958) 1 x 10^7 cells, SU-DHL-10, (ATCC CRL-2963) 1 x 10^7 cells, or SCC-3 (RRID: CVCL_1683) 1.0 x 10^7 cells with 50% matrigel (BD Biosciences). Sufficient numbers of mice were injected to achieve 8 mice per treatment arm. When tumors reached an average size of 150 to 300 mm^3, mice were randomized into treatment groups. For treatment, each therapeutic antibody (P2RY8 mAb-690 (also referred to herein as 10-0690-m), P2RY8 mAb-716 (also referred to herein as 10-0716-m or P2RY8mAb-716), P2RY8 mAb-720 (also referred to

herein as 10-0720-m), P2RY8 mAb-724 (also referred to herein as 10-0724-m), or P2RY8 mAb-729 (also referred to herein as 10-0729-m), Rituximab (anti-CD20 chimeric antibody against B cell lymphoma) and non-targeting IgG1-control (Hu-IgG) were diluted in sterile saline to a working concentration of l mg/ml for intravenous tail vein (IV) injection. Mice were treated weekly at 10 mg/kg with anti-P2RY8 antibodies or control IgG1 antibody or every 4 days at 10 mg/kg with Rituximab until the end of the experiment or for the indicated dosing duration. Tumor xenografts were measured with calipers three times per week, and tumor volume in mm^3 was determined by multiplying height x width x length. Mice were treated for 2-5 weeks. At the end of study, animals were euthanized, and tumor tissue was excised and divided to be stored as snap-frozen or formalin fixed paraffin embedded (FFPE) tissue for biomarker analysis. All animal work was carried out under a protocol approved by IACUC and the University of California at Los Angeles Animal Research Committee. Data was analyzed using StudyLog software from StudyDirector (San Francisco, CA). Results are presented as mean volumes for each group. Error bars represent the standard error (SE) of the mean.

[00217] The results of the xenograft assays are shown in Figs. 5-7. As shown in Fig. 5A and Fig. 5B, each of P2RY8 mAb-690, P2RY8 mAb-716, P2RY8 mAb-720, P2RY8 mAb-724, and P2RY8 mAb-729 directed against human P2RY8 protein as well as Rituximab, an anti-CD20 chimeric antibody, caused a substantial mean change in tumor volume at day 24, relative to control IgG1 antibody, in mice bearing P2RY8-positive human B cell lymphoma cells from SU-DHL-5 (ATCC CRL-2958) cell line. All anti-P2RY8 antibodies were found to inhibit tumor growth with P2RY8 mAb-690, P2RY8 mAb-716 and P2RY8 mAb-724 reducing tumor volume below that of the original volume at the start of the experiment. As shown in Fig. 6A and Fig. 6B, the anti-P2RY8 antibodies and Rituximab inhibited tumor growth reducing tumor volume over a 2-week period relative to control IgG1 antibody in mice bearing a different P2RY8-positive human B cell lymphoma cells from SU-DHL-10 (ATCC CRL-2963) cell line but not to the same extent as for the SU-DHL-5 cells. Inhibition of tumor cell growth in the xenograft assays by the anti-P2RY8 antibodies is dependent on presence of P2RY8 protein expression, since the antibodies failed to inhibit the growth of tumor cells from a human P2RY8-negative B-cell non-Hodgkin lymphoma cell line (SCC-3; RRID: CVCL_1683) in SCID mice.

[00218] As shown later in Table 10, the greater inhibition of SU-DHL-5 tumor cell growth relative to SU-DHL-10 by the anti-P2RY8 antibodies of the present disclosure may

be a consequence of more anti-P2RY8 antibody binding to SU-DHL-5 cells than to SU-DHL-10 cells, since the former cells are stained more by the P2RY8 antibodies than the latter cells by about 2-3 fold. This greater staining suggests that SU-DHL-5 cells may have more P2RY8 protein on its cell surface, possibly 2-3 fold higher, than SU-DHL10 cells.

[00219] Tables 1 and 25-27 provide names of expression vectors used to express the chimeric anti-P2RY8 antibodies comprising mouse heavy and light chain variable regions and human IgG1 and either human kappa or lambda light chain constant region in place of mouse heavy and light chain constant regions. Tables 2, 14-18, and 25-27 provide amino acid sequences of heavy and light chain variable regions and IMGT-defined CDRs and framework regions for a number of anti-P2RY8 antibodies including those for P2RY8 mAb-690, P2RY8 mAb-716, P2RY8 mAb-720, P2RY8 mAb-724, and P2RY8 mAb-729. The corresponding nucleic acid sequences encoding heavy and light chain variable regions are provided in Table 5 and Table 33 and the CDRs in Table 36. Table 4 and Table 32 provide amino acid sequences with Table 7 and Table 35 providing encoded nucleic acids for human IgG1 heavy chain constant region and human Ig kappa or lambda light chain constant region used to produce fully formatted full length chimeric IgG1 anti-P2RY8 antibodies.

EXAMPLE 5: HUMANIZATION OF ANTIBODIES

[00220] This example demonstrates the humanization of antibodies of the present disclosures.

[00221] Antibodies were selected for humanization analysis. The heavy chain variable (VH) and light chain variable (VL) sequences of mouse monoclonal anti-P2RY8 antibodies were compared to a library of known human germline sequences from human V_H genes and human V_L kappa genes (IMGT® the international ImMunoGeneTics information system®, World Wide Web at imgt.org; founder and director: Marie-Paule Lefranc, Montpellier, France; Giudicelli V., Duroux P., Rollin M., Aouinti S., Folch G., Jabado-Michaloud J., Lefranc M.-P., Kossida S, IMGT® Immunoinformatics Tools for Standardized V-DOMAIN Analysis. Methods Mol Biol. 2022; 2453:477-531. doi: 10.1007/978-1-0716-2115-8_24.PMID: 35622340; Lefranc M-P., IMGT® immunoglobulin repertoire analysis and antibody humanization. In: Alt, F.W, Honjo, T, Radbruch A. and Reth, M. (Eds.), Molecular Biology of B cells, Second edition, Academic Press, Elsevier Ltd, London, UK, Chapter 26, 2014, pp. 481-514. dx.doi.org, ISBN: 978-0-12-397933-9); the databases used

were IMGT human V_H genes (F+ORF, 273 germline sequences) and IMGT human V_L kappa genes (F+ORF, 74 germline sequences). The acceptor human germline was chosen from those closest in sequence to the parental antibody.

[00222] Alteration of human germline framework (i.e., non-CDR residues in VH and VL; abbreviated as FR) positions to corresponding parental murine sequence might be required to optimize binding of the humanized antibody. The sequences for versions of humanized antibodies are provided in the tables and the figures. Tables 1 and 28-31 provide names of expression vectors used to express the humanized anti-P2RY8 IgG1-kappa or -lambda antibodies comprising mouse CDR and/or its variants. Tables 3, 19-24, and 28-31 provide amino acid sequences of heavy and light chain variable regions and IMGT-defined CDRs and framework regions for a number of humanized anti-P2RY8 antibodies; corresponding nucleic acid sequences encoding heavy and light chain variable regions are provided in Tables 6 and 34 and the CDRs and framework regions in Table 37. Table 4 and Table 32 provide amino acid sequences with Tables 7 and 35 providing corresponding nucleic acid sequences for human IgG1 heavy chain constant region and human Ig kappa or lambda light chain constant region used to produce full formatted full length humanized IgG1 anti-P2RY8 antibodies.

[00223] Humanized antibodies were constructed and expressed as essentially described in Example 3. The humanized antibodies were characterized for ability to bind cells expressing P2RY8 protein by indirect immunofluorescence microscopy and flow cytometry (FACS). Endogenous P2RY8-expressing cell model (e.g., KARPAS-1106P), as well as P2RY8-overexpressing HEK293T cell lines were used to assess antibody binding to P2RY8-expressing cells. Cells not expressing P2RY8 protein (e.g., HEK293T, SCC-3 or M202 (RRID: CVCL_D746)) and parental chimeric antibodies prior to humanization were used as controls.

[00224] Figs. 8 and 9 show an example of a P2RY8-positive human large B-cell non-Hodgkin's lymphoma cell line, Karpas-1106P (RRID: CVCL_1821), stained with a chimeric anti-P2RY8 antibody, P2RY8 mAb-716 (also referred to herein as 716-m), and 7 different candidate humanized versions of P2RY8 mAb-716. Briefly, a Karpas-1106P cells grown in suspension are collected, resuspended, and incubated with candidate humanized anti-P2RY8 antibodies or control parental antibody at 20 μg/ml at 4°C for 30 min. Cells were pelleted and washed with 2% FBS-PBS to remove unbound excess antibodies. Final cell pellet is resuspended in 2% FBS-PBS, and 49 μl of cell suspension is mixed with 1 μl

of 0.3 mg/ml stock of Alexa Fluor® 647 mouse anti-human IgG-Fc secondary antibody (Biolegend, San Diego, CA; catalog #: 409320). The cells were incubated with the secondary antibody at 4°C for 30 min and then washed with 2% FBS-PBS before observing under Keyence fluorescence microscope (BZ-X710) at 40x magnification.

[00225] Fluorescence microscopy analyses revealed that among the seven candidate humanized anti-P2RY8 antibodies, derived from P2RY8 mAb-716, five of seven candidate antibodies showed good surface staining to the P2RY8 native positive cell line, as can be seen in Figs. 8 and 9. These five antibodies are indeed humanized anti-P2RY8 antibodies and are namely, P2RY8 mAb-716-h3, P2RY8 mAb-716-h4, P2RY8 mAb-716-h5, P2RY8 mAb-716-h6, and P2RY8 mAb-716-h8. Candidate antibodies, 716-h7 and 716-h9, did not stain P2RY8-expressing Karpas-1106P cells, and hence, lack P2RY8 binding activity and are not P2RY8 antibodies.

[00226] To determine relative antigen binding strengths of the humanized antibodies for binding to P2RY8 protein, indirect flow cytometry assays were performed using P2RY8 mouse monoclonal antibody P2RY8mAb-716 and its humanized P2RY8 antibodies (P2RY8mAb-716-h3 to 716-h6 as well as P2RY8mAb-716-h1 and 716-h2). Briefly, three P2RY8 native positive human lymphoma cell lines (KARPAS-1106P, SU-DHL-5, and SU-DHL-10), a P2RY8-negative human lymphoma cell line (SCC-3), and a P2RY8-negative human melanoma cell line (M202) were examined. The lymphoma cell lines grew in suspension and single cell suspensions were readily obtained. For the melanoma cell line, M202, these adherent cells were first treated with Versene® to obtain single cell suspension. Following multiple washes with 2% FBS-PBS, the cells were resuspended in 2% FBS-PBS and incubated at 4°C with P2RY8 antibodies at either 20 µg/ml or 6 µg/ml for 30 mins. Cells were pelleted and washed with 2% FBS-PBS to remove unbound excess antibodies. Final cell pellet is resuspended in 2% FBS-PBS, and 49 µl of cell suspension is mixed with 1 µl of 0.3 mg/ml stock of Alexa Fluor® 647 mouse anti-human IgG-Fc secondary antibody (Biolegend, San Diego, CA; catalog #: 409320). The cells were incubated with the secondary antibody at 4°C for 30 min. and then washed with 2% FBS-PBS. After washing with 2% FBS-PBS, the cells were subjected to flow cytometry analysis on an iQue flow cytometer (Sartorius, Goettingen, Germany) following the manufacturer protocol with Alexa Fluor® 647 fluorescent signal collected on the FL4-H channel.

[00227] As seen in Table 10, all six humanized P2RY8 antibodies (P2RY8mAb-716-h1 to 716-h6) showed good binding activities to P2RY8 native positive cell lines at both 20

μg/ml and 6 μg/ml antibody concentrations, whereas, little or no specific binding, similar to background secondary antibody control, is seen with the P2RY8-negative cell lines. The general rank order of cell-binding by P2RY8 antibodies is: Karpas-1106P ≥ SU-DHL-5 > SU-DHL-10 >>> M202, SCC-3. Compared with the P2RY8mAb-716 chimeric monoclonal antibody, humanized P2RY8 antibodies showed either similar or better antibody binding activities to native P2RY8-positive cell lines.

[00228] Similar indirect flow cytometry analysis was performed on an artificial model of P2RY8-expressing cells, a HEK293T stable cell line overexpressing human P2RY8-mGFP fusion protein (HEK293T P2RY8mGFP clone 5), and P2RY8-negative parental HEK293T cell line. As HEK293T are adherent cells, Versene® was used detach the cultured cells and obtain a single cell suspension. Furthermore, with the human P2RY8 protein expressed as a fusion protein to mGFP, the relative amount of human P2RY8 expression in HEK293T cells can be monitored based on mGFP fluorescence, which is registered in FL1-H channel of the iQue flow cytometer.

[00229] Table 11 shows all six humanized P2RY8 antibodies to have robust binding to P2RY8-overexpressing HEK293T P2RY8mGFP clone 5 stable cell line at both 20 μg/ml and 6 μg/ml antibody concentrations. Little or no binding is observed to the parental HEK293T cell line which lacks P2RY8 expression. Compared with the P2RY8mAb-716 chimeric monoclonal antibody on which the humanized P2RY8 antibodies are based, the humanized P2RY8 antibodies showed similar antibody binding activities to HEK293T P2RY8mGFP Clone 5 stable cells. Monitoring GFP fluorescence showed consistent human P2RY8-mGFP expression of the HEK293T P2RY8mGFP clone 5 cells used to compare P2RY8 antibody binding activities.

[00230] Based on the *in vitro* antigen binding data, four humanized antibodies, 10-0716-h3 (also designated as P2RY8 mAb-716-h3, P2RY8mAb-716-h3, P2RY8hAb 0716-h3, or 716-h3), 10-0716-h4 (also designated as P2RY8 mAb-716-h4, P2RY8mAb-716-h4, P2RY8hAb 0716-h4, or 716-h4), 10-0716-h5 (also designated as P2RY8 mAb-716-h5, P2RY8mAb-716-h5, P2RY8hAb 0716-h5, or 716-h5), and 10-0716-h6 (also designated as P2RY8 mAb-716-h6, P2RY8mAb-716-h6, P2RY8hAb 0716-h6, or 716-h6), were selected for further testing and development. The antibodies were derived from 10-0716-m (also designated as P2RY8 mAb-716, P2RY8mAb-716, 716-m, 716-m (hIgG1), or 0716m).

EXAMPLE 6: ANTIBODY AFFINITY MEASUREMENT BY KinExA 4000

[00231] This example demonstrates nanomolar dissociation constant (K_D) of selected humanized P2RY8 antibodies for P2RY8 protein expressed on cell surface.

[00232] Antibody equilibrium dissociation constants (K_D values) to surface protein of whole cells were measured using a KinExA 4000 (Sapidyne Instruments, Boise, ID). Briefly, PMMA beads (Sapidyne Instruments, Boise, ID; catalog #: 440176) were precoated with goat-anti-human IgG (Jackson ImmunoResearch, West Grove, PA; catalog #: 109-005-003) at 4°C overnight to a final concentration of 30 µg/ml. The beads were then blocked by the addition of bovine serum albumin (BSA; Research Products International, Mount Prospect, IL; catalog #: A30075-100.0) to 10 mg/ml and incubation at room temperature for 1 hour. P2RY8 engineered overexpression cell line HEK293T P2RY8-mGFP clone 5 cells were detached using Versene® solution (Thermo Fisher Scientific, Waltham, MA; catalog #: 15040066) and equilibrated with either 500 pM or 50 nM P2RY8 mAbs (4 humanized P2RY8 mAbs including 716-h3, 716-h4, 716-h5, 716-h6, and 716 mouse parental mAb) in 2% FBS-DMEM at 4°C overnight to reach equilibrium. Cell concentration started with $1x10^7$ cells/ml and 2-fold serial dilution was performed up to 10 points. Next day, the supernatants were saved after spinning the cells at 1500 rpm for 10 mins. The free antibody in the supernatant was detected with a fluorescent Alexa Fluor® 647 AffiniPure Goat Anti-Human IgG (Jackson ImmunoResearch, West Grove, PA; catalog #: 109-605-003) that was diluted in 1% BSA-PBS at 0.5 µg/ml. Antibody solution only (Signal 100%) and nonspecific binding (NSB, buffer only) were also included in the measurements. The K_D was calculated using these two antibody curves analyzed by the n-curve analysis from the manufacturer's software KinExA Pro Version 4.4.26.

[00233] Table 12 shows that the humanized P2RY8 antibodies, 716-h3 (P2RY8mAb-716-h3), 716-h4 h3 (P2RY8mAb-716-h4), 716-h5 (P2RY8mAb-716-h5), and 716-h6 (P2RY8mAb-716-h6), have about 4 to 6 nM dissociation constant for P2RY8 protein displayed on the surface of HEK293T cells overexpressing human P2RY8 protein (HEK293T P2RY8mGFP Clone 5 stable cell line). This single digit nanomolar K_D is nearly an order of magnitude lower than that measured for the parental 716 monoclonal antibody (P2RY8mAb-716), showing significant improvement in the binding affinity of the humanized anti-P2RY8 antibody over the original parental antibody on which the CDRs of the humanized antibodies were based. The dissociation constants of the four humanized antibodies were similar to each other.

EXAMPLE 7: GROWTH INHIBITION AND TUMOR SIZE REDUCTION BY ANTI-P2RY8 HUMANIZED ANTIBODIES IN AN *IN VIVO* XENOGRAFT MODEL

[00234] This example demonstrates inhibition of P2RY8-positive tumor cell growth and reduction in tumor size in an *in vivo* xenograft model by anti-P2RY8 humanized antibodies of the present disclosures.

[00235] *In vivo* binding studies of the four selected anti-P2RY8 humanized antibodies from Example 5 were carried out in xenograft mice injected with human cancer cell lines. Briefly, xenograft models of human cancer cell lines were established in six-week-old SCID mice (Charles River Laboratories). The following conditions were followed for subcutaneous injection of each cell line: SU-DHL-5 (ATCC CRL-2958) 1 x 10^7 cells and SCC-3 (RRID: CVCL_1683) 1.0 x 10^7 cells with 50% matrigel (BD Biosciences). Sufficient numbers of mice were injected to achieve 8 mice per treatment arm. When tumors reached an average size of 150 to 300 mm^3, mice were randomized into treatment groups. For treatment, each therapeutic antibody (humanized P2RY8 mAb-716-h3 to -h6 or chimeric P2RY8 mAb-716), Rituximab (anti-CD20 chimeric antibody against B cell lymphoma) and non-targeting IgG1-control (Hu-IgG) were diluted in sterile saline to a working concentration of 1 mg/ml for intravenous tail vein (IV) injection. Mice were treated weekly at 10 mg/kg with anti-P2RY8 antibodies or control IgG1 antibody or every 4 days at 10 mg/kg with Rituximab until the end of the experiment or for the indicated dosing duration. Tumor xenografts were measured with calipers three times per week, and tumor volume in mm^3 was determined by multiplying height x width x length. Mice were treated for 2-5 weeks. At the end of study, animals were euthanized, and tumor tissue was excised and divided to be stored as snap-frozen or formalin fixed paraffin embedded (FFPE) tissue for biomarker analysis. All animal work was carried out under a protocol approved by IACUC and the University of California at Los Angeles Animal Research Committee. Data was analyzed using StudyLog software from StudyDirector (San Francisco, CA). Results are presented as mean volumes for each group. Error bars represent the standard error (SE) of the mean.

[00236] The results of the xenograft assays are shown in Figs. 10 and 11. As shown in Fig. 10A and Fig. 10B, each of the four selected humanized anti-P2RY8 antibodies, P2RY8 mAb-716-h3, P2RY8 mAb-716-h4, P2RY8 mAb-716-h5, and P2RY8 mAb-716-h6, and chimeric parental P2RY8 mAb-716 antibody directed against human P2RY8 protein as well as Rituximab, an anti-CD20 chimeric antibody, caused a substantial mean change in tumor

volume that is observed at day 20 and continued well past the last dose at week 5, relative to control human IgG1 antibody (Hu-IgG), in mice bearing P2RY8-positive human B cell lymphoma cells from SU-DHL-5 cell line. Tumor growth in mice treated with control human IgG1 antibody reached a tumor volume of about 3000 mm^3, requiring euthanizing the mice on about day 18.

[00237] The anti-P2RY8 antibodies and Rituximab inhibited tumor growth reducing tumor volume relative to control IgG1 antibody over the duration of the experiment, about 54-62 day period (Fig. 10A). Notable are humanized P2RY8 mAb-716-h6 and chimeric P2RY8 mAb-716 antibodies which inhibited tumor growth such that at the end of the study period on either day 54 or 62, the tumor volume remained the same as the starting tumor volume at day 0. Most notably is the humanized P2RY8 antibody, P2RY8 mAb-716-h3, which reduced tumor volume below its original size to an almost undectable tumor mass (Fig. 10A), making the humanized P2RY8 mAb-716-h3 antibody the lead antibody among the four selected humanized anti-P2RY8 antibodies.

[00238] Amino acid sequence of P2RY8 mAb-716-h3 (also referred to herein as P2RY8mAb-716-h3, P2RY8hAb 0716-h3, 10-0716-h3, or 716-h3) heavy and light chain variable regions are provided as SEQ ID NOs: 177 and 185, respectively. The IMGT-defined CDR1 (SEQ ID NO: 186), CDR2 (SEQ ID NO: 187) and CDR3 (SEQ ID NO: 188) of the 10-0716-h3 light chain variable region are identical to the light chain IMGT-defined CDRs (SEQ ID NOs: 58-60) of the chimeric P2RY8 mAb-716 (also referred to herein as 10-0716-m, 0716m or 716-m) antibody on which the CDRs of the 10-0716-h3 light chain variable region are based. The IMGT-defined CDR3 (SEQ ID NO: 180) of the 10-0716-h3 heavy chain variable region is identical to the heavy chain IMGT-defined CDR3 (SEQ ID NOs: 58-60) of the chimeric P2RY8 mAb-716 antibody. For the IMGT-defined CDR1 (SEQ ID NO: 178) and CDR2 (SEQ ID NO: 179) of the 10-0716-h3 heavy chain variable region, these two heavy chain CDRs are variants of the heavy chain IMGT-defined CDR1 (SEQ ID NO: 50) and CDR2 (SEQ ID NO: 51) of the chimeric P2RY8 mAb-716 antibody. A single amino acid difference exists at the very first amino acid of each CDR, wherein alanine is replaced with glycine to obtain heavy chain CDR1 and valine is replaced with isoleucine to obtain heavy chain CDR2 of 10-0716-h3 humanized anti-P2RY8 antibody.

[00239] The expression vector p10-0716-h3 used to express P2RY8 mAb-716-h3 humanized anti-P2RY8 antibody was deposited with the American Type Culture

Collection (ATCC), 10801 University Boulevard, Manassas, Virginia 20110-2209, on November 14, 2024, and assigned Accession Number PTA-127827. This deposit will be maintained under the terms of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the Purposes of Patent Procedure.

[00240] Inhibition of tumor cell growth and/or reduction in tumor volume in the xenograft assays by the anti-P2RY8 antibodies is dependent on presence of P2RY8 protein expression, since the antibodies lacked any significant effect on growth of tumor cells from a human P2RY8-negative B-cell non-Hodgkin lymphoma cell line (SCC-3; RRID: CVCL_1683) in SCID mice (Fig. 11).

EXAMPLE 8: INTERNALIZATION OF CHIMERIC AND HUMANIZED ANTI-P2RY8 IgG1 ANTIBODIES

[00241] This example demonstrates the internalization of anti-P2RY8 antibodies of the present disclosures.

[00242] Primary antibodies were labeled with Alexa Fluor® 647 Antibody Labeling Kit (ThermoFisher Scientific, Waltham, MA; catalog #: A20006). For antibody internalization studies, P2RY8-positive Karpas-1106P and SU-DHL-5 were cultured in Ibidi USA μ-SLIDE 4 Well chamber (FisherScientific, Pittsburgh, PA; catalog #: NC0515977); HEK293T was cultured in the Ibidi chamber slides and transfected with P2RY8mGFP fusion protein expression vector. Hoechst 33342 DNA dye was used for nucleus staining (Abcam, Waltham, MA; catalog #: ab228551, 1 μM final concentration). Cells were stained with 25 μg/ml antibody and a time course of images were taken until internalization was complete using the Keyence fluorescence microscope (BZ-X710).

[00243] Figs. 12-15 show rapid internalization of the chimeric P2RY8 mAb-716 (also referred to herein as 0716m) in P2RY8-positive Karpas-1106P cells (Figs. 12 and 13), P2RY8-positive SU-DHL-5 cells (Fig. 14) and P2RY8-positive HEK293T cells (Fig. 15) successfully transfected with the P2RY8mGFP fusion protein expression vector. Note initial peripheral staining of the cell surface by the P2RY8 antibody (red for AF647 fluorescence), which in many cases are uniform, followed by loss or uneven peripheral staining and an increase in punctate staining in interior of the cell. Location of the nucleus is shown as blue in Figs. 12 and 15, and GFP fluorescence is shown as green in Fig. 15 (last two timepoints). Phase contrast overlays on fluorescence images are shown in Fig. 12 (two bottom panels), Fig. 13 (bottom panel) and Fig. 14 bottom panel). Thus, the observed

internalization of the chimeric P2RY8 mAb-716 in P2RY8-positive Karpas-1106P cells is consistent with the ability of P2RY8 antibody to induce rapid internalization of the P2RY8 protein/chimeric P2RY8 mAb-716 antibody complex in P2RY8-positive cancer cells.

[00244] Internalization of the lead humanized anti-P2RY8 antibody was also studied in P2RY8-positive Karpas-1106P lymphoma cells. As seen in Fig. 16, the lead humanized anti-P2RY8 antibody, P2RY8 mAb-716-h3, can undergo rapid internalization following binding of cell surface-exposed P2RY8 protein. Binding of the P2RY8 antibodies of the present disclosure may induce rapid internalization of the P2RY8 protein/humanized P2RY8 antibody complex in P2RY8-positive cancer cells, as observed for P2RY8-positive Karpas-1106P lymphoma cells. Overlays of AF647 fluorescence corresponding to location of P2RY8 mAb-716-h3 antibody on a phase contrast image for a field of Karpas-1106P cells are shown for the last four timepoints (last four panels).

EXAMPLE 9: SPECIES SPECIFICITY OF LEAD ANTIBODY

[00245] This example demonstrates the binding specificity of the lead humanized anti-P2RY8 antibody, P2RY8 mAb-716-h3, for human and crab-eating macaque P2RY8 protein.

[00246] Primary antibodies were labeled with Alexa Fluor® 647 Antibody Labeling Kit (ThermoFisher Scientific, Waltham, MA; catalog #: A20006). For antibody internalization, immunofluorescence assay using Alexa Fluor® 647 goat anti-mouse IgG (minimal x-reactivity) secondary antibody (Biolegend, San Diego, CA; catalog #: 405322). The lead humanized anti-P2RY8 antibody, P2RY8 mAb-716-h3, was used in an indirect flow cytometry assay to quantitate binding of the lead antibody to human, crab-eating macaque and dog P2RY8 protein expressed on the surface of HEK293T cells. HEK293T cells engineered to stably express human P2RY8 fused to GFP, crab-eating macaque P2RY8 fused to GFP, or dog P2RY8 fused to GFP were used as artificial models of P2RY8 expression (Table 39). The cells were detached from the surface of the culture flasks by Versene® (instead of trypsin) to protect the cell surface proteins and obtain single cell suspension. The cells were collected, washed, resuspended in 2% FBS-PBS and incubated at 4°C with P2RY8 mAb-716-h3 antibody at 4 µg/ml for 30 mins. Cells were pelleted and washed with 2% FBS-PBS to remove unbound excess antibodies. Final cell pellet is resuspended in 2% FBS-PBS, and 49 µl of cell suspension is mixed with 1 µl of 0.3 mg/ml stock of Alexa Fluor® 647 mouse anti-human IgG-Fc secondary antibody (Biolegend, San Diego, CA; catalog #: 409320). The cells were incubated with the secondary antibody at

4°C for 30 min. and then washed with 2% FBS-PBS. After washing with 2% FBS-PBS, the cells were subjected to flow cytometry analysis on a BD Accuri™ C6 flow cytometer. The FL4-H channel is used to collect the AF647 fluorescent signal, while the FL1-H channel is used to collect the GFP fluorescent signal. Negative controls are P2RY8-negative HEK293T cells (HEK203T parental), incubation only with secondary AF647-labeled anti-human IgG-Fc secondary antibody (anti-human 2° only), and incubation with no antibody (no antibody).

[00247] Table 13 shows that the lead anti-P2RY8 antibody, P2RY8 mAb-716-h3, binds human P2RY8-expressing HEK293T cells (HEK293T human P2RY8 mGFP Clone5) as expected. In addition, the antibody also binds HEK293T cells expressing crab-eating macaque P2RY8 protein (610-HEK293T macP2RY8 mGFP mass pop) but does not bind or has little affinity for HEK293T cells expressing dog P2RY8 protein (618-HEK293T dogP2RY8 mGFP pop). Subtracting for background binding (anti-human 2° only) and normalizing for amount of expression of the P2RY8-mGFP fusion protein (GFP signal in the 716-h3 column), the binding affinity of the lead antibody for the human P2RY8 protein may be estimated to be about 330-fold greater than its affinity for the dog P2RY8 protein. Thus, the P2RY8 mAb-716-h3 lead antibody binds with good affinity, previously characterized to be in the nanomolar range (see Table 12), but does not bind or has little binding affinity for dog P2RY8 protein.

Table 2: Exemplary Mouse V_H, Mouse V_L, and CDR sequences of chimeric P2RY8 antibodies

Seq ID NO.:	Name	Sequence
1	10-0690-m_VH	DVQLQESGPGLVKPSQSLSLTCIVTGYSITSDYAWNWIRQFPGNKLE WMGYIDYSGSTSYNPSLKSRVSITRDTSKNQFFLQLNSVTTEDAATYY CTRGFWYFDVWGAGTTVTVSS
2	10-0690-m_VH - IMGT_CDR1	GYSITSDYA
3	10-0690-m_VH - IMGT_CDR2	IDYSGST
4	10-0690-m_VH - IMGT_CDR3	TRGFWYFDV
5	10-0690-m_VH - IMGT_FR1	DVQLQESGPGLVKPSQSLSLTCIVT

6	10-0690-m_VH - IMGT_FR2	WNWIRQFPGNKLEWMGY
7	10-0690-m_VH - IMGT_FR3	SYNPSLKSRVSITRDTSKNQFFLQLNSVTTEDAATYYC
8	10-0690-m_VH - IMGT_FR4	WGAGTTVTVSS
9	10-0690-m_VL	DIVLTQYPASLAVSLGQRATISCRASESVDSYGYTFMHWYQQKPGQP PKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQSNE DPFTFGSGTKLEIK
10	10-0690-m_VL - IMGT_CDR1	ESVDSYGYTF
11	10-0690-m_VL - IMGT_CDR2	RAS
12	10-0690-m_VL - IMGT_CDR3	QQSNEDPFT
13	10-0690-m_VL - IMGT_FR1	DIVLTQYPASLAVSLGQRATISCRAS
14	10-0690-m_VL - IMGT_FR2	MHWYQQKPGQPPKLLIY
15	10-0690-m_VL - IMGT_FR3	NLESGIPARFSGSGSRTDFTLTINPVEADDVATYYC
16	10-0690-m_VL - IMGT_FR4	FGSGTKLEIK
	Name	Sequence
17	10-0695-m_VH	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLE WMGYISYSGSTSYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYYC ARGYWYFDVWGAGTTVTVSS
18	10-0695-m_VH - IMGT_CDR1	GYSITSDYA
19	10-0695-m_VH - IMGT_CDR2	ISYSGST
20	10-0695-m_VH - IMGT_CDR3	ARGYWYFDV
21	10-0695-m_VH - IMGT_FR1	DVQLQESGPGLVKPSQSLSLTCTVT
22	10-0695-m_VH - IMGT_FR2	WNWIRQFPGNKLEWMGY
23	10-0695-m_VH - IMGT_FR3	SYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYYC
24	10-0695-m_VH - IMGT_FR4	WGAGTTVTVSS
25	10-0695-m_VL	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYSFMHWYQQKPGQP PKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQSNE DPYTFGGGTKLEIK
26	10-0695-m_VL - IMGT_CDR1	ESVDSYGYSF

27	10-0695-m_VL - IMGT_CDR2	RAS
28	10-0695-m_VL - IMGT_CDR3	QQSNEDPYT
29	10-0695-m_VL - IMGT_FR1	DIVLTQSPASLAVSLGQRATISCRAS
30	10-0695-m_VL - IMGT_FR2	MHWYQQKPGQPPKLLIY
31	10-0695-m_VL - IMGT_FR3	NLESGIPARFSGSGSRTDFTLTINPVEADDVATYYC
32	10-0695-m_VL - IMGT_FR4	FGGGTKLEIK
	Name	**Sequence**
33	10-0701-m_VH	EVQLQQSGPELVKPGASMKISCKASSSSFTGYTMNWVKQSHGKNLE WIGLINPYNGGTTYNQKFKGKATLTVDKSSSTAYMELLSLTSEDSAVY YCARGRAYVNPGDYAMDYWGQGTSVTVSS
34	10-0701-m_VH - IMGT_CDR1	SSSFTGYT
35	10-0701-m_VH - IMGT_CDR2	INPYNGGT
36	10-0701-m_VH - IMGT_CDR3	ARGRAYVNPGDYAMDY
37	10-0701-m_VH - IMGT_FR1	EVQLQQSGPELVKPGASMKISCKAS
38	10-0701-m_VH - IMGT_FR2	MNWVKQSHGKNLEWIGL
39	10-0701-m_VH - IMGT_FR3	TYNQKFKGKATLTVDKSSSTAYMELLSLTSEDSAVYYC
40	10-0701-m_VH - IMGT_FR4	WGQGTSVTVSS
41	10-0701-m_VL	QIVLTQSPAIMSASLGERVTMTCTASSSASSSYLHWYQQKPGSSPKL WIYSTSNLASGVPARFSGSGSGTSYSLTIRSMEAEDAATYYCHQYHRS PYTFGGGTKLEIK
42	10-0701-m_VL - IMGT_CDR1	SSASSSY
43	10-0701-m_VL - IMGT_CDR2	STS
44	10-0701-m_VL - IMGT_CDR3	HQYHRSPYT
45	10-0701-m_VL - IMGT_FR1	QIVLTQSPAIMSASLGERVTMTCTAS
46	10-0701-m_VL - IMGT_FR2	LHWYQQKPGSSPKLWIY
47	10-0701-m_VL - IMGT_FR3	NLASGVPARFSGSGSGTSYSLTIRSMEAEDAATYYC
48	10-0701-m_VL - IMGT_FR4	FGGGTKLEIK

	Name	Sequence
49	10-0716-m_VH	DVHLQESGPGLVKPSQSLSLTCTVTAYSITSDYAWNWIRQFPGNKLE WMGYVTYSGTTTYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYFC ARGYWYFDVWGAGTTVTVSS
50	10-0716-m_VH - IMGT_CDR1	AYSITSDYA
51	10-0716-m_VH - IMGT_CDR2	VTYSGTT
52	10-0716-m_VH - IMGT_CDR3	ARGYWYFDV
53	10-0716-m_VH - IMGT_FR1	DVHLQESGPGLVKPSQSLSLTCTVT
54	10-0716-m_VH - IMGT_FR2	WNWIRQFPGNKLEWMGY
55	10-0716-m_VH - IMGT_FR3	TYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATYFC
56	10-0716-m_VH - IMGT_FR4	WGAGTTVTVSS
57	10-0716-m_VL	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYTFMHWYQQKPGQP PKLLIYRASNVHSGIPARFSASGSRTDFTLTINPVEADDIATYYCQQSNE DPFTFGSGTNLEIK
58	10-0716-m_VL - IMGT_CDR1	ESVDSYGYTF
59	10-0716-m_VL - IMGT_CDR2	RAS
60	10-0716-m_VL - IMGT_CDR3	QQSNEDPFT
61	10-0716-m_VL - IMGT_FR1	DIVLTQSPASLAVSLGQRATISCRAS
62	10-0716-m_VL - IMGT_FR2	MHWYQQKPGQPPKLLIY
63	10-0716-m_VL - IMGT_FR3	NVHSGIPARFSASGSRTDFTLTINPVEADDIATYYC
64	10-0716-m_VL - IMGT_FR4	FGSGTNLEIK
	Name	**Sequence**
65	10-0720-m_VH	DVQFQESGPGLVKPSQSQSLTCTVTGYSITSDYAWNWLRQFPGNKLE WMGYISYSGTTNYNPSLKSRISITRDTSKNQFFLQLNSVTSEDTATYYC ARGYWYFDVWGAGTTVTVSS
66	10-0720-m_VH - IMGT_CDR1	GYSITSDYA
67	10-0720-m_VH - IMGT_CDR2	ISYSGTT
68	10-0720-m_VH - IMGT_CDR3	ARGYWYFDV
69	10-0720-m_VH - IMGT_FR1	DVQFQESGPGLVKPSQSQSLTCTVT

70	10-0720-m_VH - IMGT_FR2	WNWLRQFPGNKLEWMGY
71	10-0720-m_VH - IMGT_FR3	NYNPSLKSRISITRDTSKNQFFLQLNSVTSEDTATYYC
72	10-0720-m_VH - IMGT_FR4	WGAGTTVTVSS
73	10-0720-m_VL	DIVLTQSPASLAVSLGQRATISCRASERVDSYGYTFMHWYQQKPGQP PKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQSNE DPFTFGGGTKLEIK
74	10-0720-m_VL - IMGT_CDR1	ERVDSYGYTF
75	10-0720-m_VL - IMGT_CDR2	RAS
76	10-0720-m_VL - IMGT_CDR3	QQSNEDPFT
77	10-0720-m_VL - IMGT_FR1	DIVLTQSPASLAVSLGQRATISCRAS
78	10-0720-m_VL - IMGT_FR2	MHWYQQKPGQPPKLLIY
79	10-0720-m_VL - IMGT_FR3	NLESGIPARFSGSGSRTDFTLTINPVEADDVATYYC
80	10-0720-m_VL - IMGT_FR4	FGGGTKLEIK
	Name	**Sequence**
81	10-0724-m_VH	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLE WMGYITYSGTTRYNPSLKSRISITRDTSKNHFFLQLSSLTTEDTATYYCA RGFWYFDVWGAGTAVTVSS
82	10-0724-m_VH - IMGT_CDR1	GYSITSDYA
83	10-0724-m_VH - IMGT_CDR2	ITYSGTT
84	10-0724-m_VH - IMGT_CDR3	ARGFWYFDV
85	10-0724-m_VH - IMGT_FR1	DVQLQESGPGLVKPSQSLSLTCTVT
86	10-0724-m_VH - IMGT_FR2	WNWIRQFPGNKLEWMGY
87	10-0724-m_VH - IMGT_FR3	RYNPSLKSRISITRDTSKNHFFLQLSSLTTEDTATYYC
88	10-0724-m_VH - IMGT_FR4	WGAGTAVTVSS
89	10-0724-m_VL	DIVLTQSPASLAVSLGQRATISCRASESVDTYGYNFLHWYQQKPGQPP KLLIYRASNLQSGIPARFSGSGSRADFTLTINPVEADDVATYYCQQSNE DLLTIGGGTKLEIK
90	10-0724-m_VL - IMGT_CDR1	ESVDTYGYNF

91	10-0724-m_VL - IMGT_CDR2	RAS
92	10-0724-m_VL - IMGT_CDR3	QQSNEDLLT
93	10-0724-m_VL - IMGT_FR1	DIVLTQSPASLAVSLGQRATISCRAS
94	10-0724-m_VL - IMGT_FR2	LHWYQQKPGQPPKLLIY
95	10-0724-m_VL - IMGT_FR3	NLQSGIPARFSGSGSRADFTLTINPVEADDVATYYC
96	10-0724-m_VL - IMGT_FR4	IGGGTKLEIK
	Name	**Sequence**
97	10-0725-m_VH	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKLE WMGYITYSGTTRYNPSLKSRISITRDTSKNHFFLQLSSLTTEDTATYYCA RGFWYFDVWGAGTAVTVSS
98	10-0725-m_VH - IMGT_CDR1	GYSITSDYA
99	10-0725-m_VH - IMGT_CDR2	ITYSGTT
100	10-0725-m_VH - IMGT_CDR3	ARGFWYFDV
101	10-0725-m_VH - IMGT_FR1	DVQLQESGPGLVKPSQSLSLTCTVT
102	10-0725-m_VH - IMGT_FR2	WNWIRQFPGNKLEWMGY
103	10-0725-m_VH - IMGT_FR3	RYNPSLKSRISITRDTSKNHFFLQLSSLTTEDTATYYC
104	10-0725-m_VH - IMGT_FR4	WGAGTAVTVSS
105	10-0725-m_VL	QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDHLFT GLIGGTNNRAPGVPARFSGSLIGDKAALTITGAQTEDEAIYFCALWYS NHWVFGGGTKLTVL
106	10-0725-m_VL - IMGT_CDR1	TGAVTTSNY
107	10-0725-m_VL - IMGT_CDR2	GTN
108	10-0725-m_VL - IMGT_CDR3	ALWYSNHWV
109	10-0725-m_VL - IMGT_FR1	QAVVTQESALTTSPGETVTLTCRSS
110	10-0725-m_VL - IMGT_FR2	ANWVQEKPDHLFTGLIG
111	10-0725-m_VL - IMGT_FR3	NRAPGVPARFSGSLIGDKAALTITGAQTEDEAIYFC
112	10-0725-m_VL - IMGT_FR4	FGGGTKLTVL

	Name	Sequence
113	10-0728-m_VH	EVKLEESGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRQSPEKGL EWVAEIRSKANNHATYYAESVKGRFTISRDDSKSSVYLQMNSLRAEDT GIYYCTGFMITTAWFAYWGQGTLVTVSS
114	10-0728-m_VH - IMGT_CDR1	GFTFSDAW
115	10-0728-m_VH - IMGT_CDR2	IRSKANNHAT
116	10-0728-m_VH - IMGT_CDR3	TGFMITTAWFAY
117	10-0728-m_VH - IMGT_FR1	EVKLEESGGGLVQPGGSMKLSCAAS
118	10-0728-m_VH - IMGT_FR2	MDWVRQSPEKGLEWVAE
119	10-0728-m_VH - IMGT_FR3	YYAESVKGRFTISRDDSKSSVYLQMNSLRAEDTGIYYC
120	10-0728-m_VH - IMGT_FR4	WGQGTLVTVSS
121	10-0728-m_VL	ENVLTQSPAIMSASLGEKVTMSCRASSSVNYMYWYQQKSDASPKLW IYYTSNLAPGVPARFSGSGSGNSYSLTISSMEGEDAATYYCQQFTSSPY TFGGGTKLEIK
122	10-0728-m_VL - IMGT_CDR1	SSVNY
123	10-0728-m_VL - IMGT_CDR2	YTS
124	10-0728-m_VL - IMGT_CDR3	QQFTSSPYT
125	10-0728-m_VL - IMGT_FR1	ENVLTQSPAIMSASLGEKVTMSCRAS
126	10-0728-m_VL - IMGT_FR2	MYWYQQKSDASPKLWIY
127	10-0728-m_VL - IMGT_FR3	NLAPGVPARFSGSGSGNSYSLTISSMEGEDAATYYC
128	10-0728-m_VL - IMGT_FR4	FGGGTKLEIK
	Name	**Sequence**
129	10-0729-m_VH	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDFAWNWIRQVPGNKLE WMGYISYSGTTRYNPFLKSRISITRDTSKNQFFLQLNSVTPEDTATYYC ARGYWYFDVWGAGTTVTVSS
130	10-0729-m_VH - IMGT_CDR1	GYSITSDFA
131	10-0729-m_VH - IMGT_CDR2	ISYSGTT
132	10-0729-m_VH - IMGT_CDR3	ARGYWYFDV
133	10-0729-m_VH - IMGT_FR1	DVQLQESGPGLVKPSQSLSLTCTVT

134	10-0729-m_VH - IMGT_FR2	WNWIRQVPGNKLEWMGY
135	10-0729-m_VH - IMGT_FR3	RYNPFLKSRISITRDTSKNQFFLQLNSVTPEDTATYYC
136	10-0729-m_VH - IMGT_FR4	WGAGTTVTVSS
137	10-0729-m_VL	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYTFMHWYQHKPGQS PKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQSN DDPYTFGGGTQLEVK
138	10-0729-m_VL - IMGT_CDR1	ESVDSYGYTF
139	10-0729-m_VL - IMGT_CDR2	RAS
140	10-0729-m_VL - IMGT_CDR3	QQSNDDPYT
141	10-0729-m_VL - IMGT_FR1	DIVLTQSPASLAVSLGQRATISCRAS
142	10-0729-m_VL - IMGT_FR2	MHWYQHKPGQSPKLLIY
143	10-0729-m_VL - IMGT_FR3	NLESGIPARFSGSGSRTDFTLTINPVEADDVATYYC
144	10-0729-m_VL - IMGT_FR4	FGGGTQLEVK

Table 3: Exemplary Humanized V_H, Humanized V_L, and CDR sequences of humanized P2RY8 antibodies

Seq ID NO. :	Name	Sequence
145	10-0716-h1_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC ARGYWYFDVWGQGTTVTVSS
146	10-0716-h1_VH - IMGT_CDR1	GYSITSDYA
147	10-0716-h1_VH - IMGT_CDR2	ITYSGTT
148	10-0716-h1_VH - IMGT_CDR3	ARGYWYFDV
149	10-0716-h1_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
150	10-0716-h1_VH - IMGT_FR2	WNWIRQAPGKGLEWVSY
151	10-0716-h1_VH - IMGT_FR3	TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC

152	10-0716-h1_VH - IMGT_FR4	WGQGTTVTVSS
153	10-0716-h1_VL	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGK APKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSN EDPFTFGQGTKLEIK
154	10-0716-h1_VL - IMGT_CDR1	ESVDSYGYTF
155	10-0716-h1_VL - IMGT_CDR2	RAS
156	10-0716-h1_VL - IMGT_CDR3	QQSNEDPFT
157	10-0716-h1_VL - IMGT_FR1	DIQMTQSPSSLSASVGDRVTITCRAS
158	10-0716-h1_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
159	10-0716-h1_VL - IMGT_FR3	NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
160	10-0716-h1_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
161	10-0716-h2_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC ARGYWYFDVWGQGTTVTVSS
162	10-0716-h2_VH - IMGT_CDR1	GYSITSDYA
163	10-0716-h2_VH - IMGT_CDR2	ITYSGTT
164	10-0716-h2_VH - IMGT_CDR3	ARGYWYFDV
165	10-0716-h2_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
166	10-0716-h2_VH - IMGT_FR2	WNWIRQAPGKGLEWVSY
167	10-0716-h2_VH - IMGT_FR3	TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC
168	10-0716-h2_VH - IMGT_FR4	WGQGTTVTVSS
169	10-0716-h2_VL	DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKA PKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNE DPFTFGQGTKLEIK
170	10-0716-h2_VL - IMGT_CDR1	ESVDSYGYTF
171	10-0716-h2_VL - IMGT_CDR2	RAS

172	10-0716-h2_VL - IMGT_CDR3	QQSNEDPFT
173	10-0716-h2_VL - IMGT_FR1	DIQLTQSPSSLSASVGDRATITCRAS
174	10-0716-h2_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
175	10-0716-h2_VL - IMGT_FR3	NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC
176	10-0716-h2_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
177	10-0716-h3_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDVWGQGTTVTVSS
178	10-0716-h3_VH - IMGT_CDR1	GYSITSDYA
179	10-0716-h3_VH - IMGT_CDR2	ITYSGTT
180	10-0716-h3_VH - IMGT_CDR3	ARGYWYFDV
181	10-0716-h3_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
182	10-0716-h3_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
183	10-0716-h3_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
184	10-0716-h3_VH - IMGT_FR4	WGQGTTVTVSS
185	10-0716-h3_VL	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKLEIK
186	10-0716-h3_VL - IMGT_CDR1	ESVDSYGYTF
187	10-0716-h3_VL - IMGT_CDR2	RAS
188	10-0716-h3_VL - IMGT_CDR3	QQSNEDPFT
189	10-0716-h3_VL - IMGT_FR1	DIQMTQSPSSLSASVGDRVTITCRAS
190	10-0716-h3_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
191	10-0716-h3_VL - IMGT_FR3	NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
192	10-0716-h3_VL - IMGT_FR4	FGQGTKLEIK

	Name	Sequence
193	10-0716-h4_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC ARGYWYFDVWGQGTTVTVSS
194	10-0716-h4_VH - IMGT_CDR1	GYSITSDYA
195	10-0716-h4_VH - IMGT_CDR2	ITYSGTT
196	10-0716-h4_VH - IMGT_CDR3	ARGYWYFDV
197	10-0716-h4_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
198	10-0716-h4_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
199	10-0716-h4_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
200	10-0716-h4_VH - IMGT_FR4	WGQGTTVTVSS
201	10-0716-h4_VL	DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKA PKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNE DPFTFGQGTKLEIK
202	10-0716-h4_VL - IMGT_CDR1	ESVDSYGYTF
203	10-0716-h4_VL - IMGT_CDR2	RAS
204	10-0716-h4_VL - IMGT_CDR3	QQSNEDPFT
205	10-0716-h4_VL - IMGT_FR1	DIQLTQSPSSLSASVGDRATITCRAS
206	10-0716-h4_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
207	10-0716-h4_VL - IMGT_FR3	NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC
208	10-0716-h4_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
209	10-0716-h5_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC ARGYWYFDVWGQGTTVTVSS
210	10-0716-h5_VH - IMGT_CDR1	GYSITSDYA
211	10-0716-h5_VH - IMGT_CDR2	ITYSGTT
212	10-0716-h5_VH - IMGT_CDR3	ARGYWYFDV

213	10-0716-h5_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
214	10-0716-h5_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
215	10-0716-h5_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
216	10-0716-h5_VH - IMGT_FR4	WGQGTTVTVSS
217	10-0716-h5_VL	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGK APKLLIYRASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSN EDPFTFGQGTKLEIK
218	10-0716-h5_VL - IMGT_CDR1	ESVDSYGYTF
219	10-0716-h5_VL - IMGT_CDR2	RAS
220	10-0716-h5_VL - IMGT_CDR3	QQSNEDPFT
221	10-0716-h5_VL - IMGT_FR1	DIQMTQSPSSLSASVGDRVTITCRAS
222	10-0716-h5_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
223	10-0716-h5_VL - IMGT_FR3	NVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYC
224	10-0716-h5_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
225	10-0716-h6_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC ARGYWYFDVWGQGTTVTVSS
226	10-0716-h6_VH - IMGT_CDR1	GYSITSDYA
227	10-0716-h6_VH - IMGT_CDR2	ITYSGTT
228	10-0716-h6_VH - IMGT_CDR3	ARGYWYFDV
229	10-0716-h6_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
230	10-0716-h6_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
231	10-0716-h6_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
232	10-0716-h6_VH - IMGT_FR4	WGQGTTVTVSS

233	10-0716-h6_VL	DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYRASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEIK
234	10-0716-h6_VL - IMGT_CDR1	ESVDSYGYTF
235	10-0716-h6_VL - IMGT_CDR2	RAS
236	10-0716-h6_VL - IMGT_CDR3	QQSNEDPFT
237	10-0716-h6_VL - IMGT_FR1	DIQLTQSPSSLSASVGDRATITCRAS
238	10-0716-h6_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
239	10-0716-h6_VL - IMGT_FR3	NVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC
240	10-0716-h6_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
241	10-0716-h8_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYITYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDVWGQGTTVTVSS
242	10-0716-h8_VH - IMGT_CDR1	GYSITSDYA
243	10-0716-h8_VH - IMGT_CDR2	ITYSGTT
244	10-0716-h8_VH - IMGT_CDR3	ARGYWYFDV
245	10-0716-h8_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
246	10-0716-h8_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
247	10-0716-h8_VH - IMGT_FR3	TYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYC
248	10-0716-h8_VH - IMGT_FR4	WGQGTTVTVSS
249	10-0716-h8_VL	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKLEIK
250	10-0716-h8_VL - IMGT_CDR1	ESVDSYGYTF
251	10-0716-h8_VL - IMGT_CDR2	RAS
252	10-0716-h8_VL - IMGT_CDR3	QQSNEDPFT

253	10-0716-h8_VL - IMGT_FR1	DIQMTQSPSSLSASVGDRVTITCRAS
254	10-0716-h8_VL - IMGT_FR2	MHWYQQKPGKAPKLLIY
255	10-0716-h8_VL - IMGT_FR3	NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
256	10-0716-h8_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
257	10-0724-h3_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGFWYFDVWGQGTTVTVSS
258	10-0724-h3_VH - IMGT_CDR1	GYSITSDYA
259	10-0724-h3_VH - IMGT_CDR2	ITYSGTT
260	10-0724-h3_VH - IMGT_CDR3	ARGFWYFDV
261	10-0724-h3_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
262	10-0724-h3_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
263	10-0724-h3_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
264	10-0724-h3_VH - IMGT_FR4	WGQGTTVTVSS
265	10-0724-h3_VL	DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKPGKAPKLLIYRASNVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDLLTFGQGTKLEIK
266	10-0724-h3_VL - IMGT_CDR1	ESVDTYGYNF
267	10-0724-h3_VL - IMGT_CDR2	RAS
268	10-0724-h3_VL - IMGT_CDR3	QQSNEDLLT
269	10-0724-h3_VL - IMGT_FR1	DIQMTQSPSSLSASVGDRVTITCRAS
270	10-0724-h3_VL - IMGT_FR2	LHWYQQKPGKAPKLLIY
271	10-0724-h3_VL - IMGT_FR3	NVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
272	10-0724-h3_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**

273	10-0724-h4_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC ARGFWYFDVWGQGTTVTVSS
274	10-0724-h4_VH - IMGT_CDR1	GYSITSDYA
275	10-0724-h4_VH - IMGT_CDR2	ITYSGTT
276	10-0724-h4_VH - IMGT_CDR3	ARGFWYFDV
277	10-0724-h4_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
278	10-0724-h4_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
279	10-0724-h4_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
280	10-0724-h4_VH - IMGT_FR4	WGQGTTVTVSS
281	10-0724-h4_VL	DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGKAP KLLIYRASNVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNE DLLTFGQGTKLEIK
282	10-0724-h4_VL - IMGT_CDR1	ESVDTYGYNF
283	10-0724-h4_VL - IMGT_CDR2	RAS
284	10-0724-h4_VL - IMGT_CDR3	QQSNEDLLT
285	10-0724-h4_VL - IMGT_FR1	DIQLTQSPSSLSASVGDRATITCRAS
286	10-0724-h4_VL - IMGT_FR2	LHWYQQKPGKAPKLLIY
287	10-0724-h4_VL - IMGT_FR3	NVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC
288	10-0724-h4_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
289	10-0724-h5_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC ARGFWYFDVWGQGTTVTVSS
290	10-0724-h5_VH - IMGT_CDR1	GYSITSDYA
291	10-0724-h5_VH - IMGT_CDR2	ITYSGTT
292	10-0724-h5_VH - IMGT_CDR3	ARGFWYFDV

293	10-0724-h5_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
294	10-0724-h5_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
295	10-0724-h5_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
296	10-0724-h5_VH - IMGT_FR4	WGQGTTVTVSS
297	10-0724-h5_VL	DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKPGKA PKLLIYRASNVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNE DLLTFGQGTKLEIK
298	10-0724-h5_VL - IMGT_CDR1	ESVDTYGYNF
299	10-0724-h5_VL - IMGT_CDR2	RAS
300	10-0724-h5_VL - IMGT_CDR3	QQSNEDLLT
301	10-0724-h5_VL - IMGT_FR1	DIQMTQSPSSLSASVGDRVTITCRAS
302	10-0724-h5_VL - IMGT_FR2	LHWYQQKPGKAPKLLIY
303	10-0724-h5_VL - IMGT_FR3	NVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATYYC
304	10-0724-h5_VL - IMGT_FR4	FGQGTKLEIK
	Name	**Sequence**
305	10-0724-h6_VH	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLE WMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC ARGFWYFDVWGQGTTVTVSS
306	10-0724-h6_VH - IMGT_CDR1	GYSITSDYA
307	10-0724-h6_VH - IMGT_CDR2	ITYSGTT
308	10-0724-h6_VH - IMGT_CDR3	ARGFWYFDV
309	10-0724-h6_VH - IMGT_FR1	EVQLVESGGGLVQPGGSLRLSCAVS
310	10-0724-h6_VH - IMGT_FR2	WNWIRQAPGKGLEWMGY
311	10-0724-h6_VH - IMGT_FR3	TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC
312	10-0724-h6_VH - IMGT_FR4	WGQGTTVTVSS

313	10-0724-h6_VL	DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGKAPKLLIYRASNVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDLLTFGQGTKLEIK
314	10-0724-h6_VL - IMGT_CDR1	ESVDTYGYNF
315	10-0724-h6_VL - IMGT_CDR2	RAS
316	10-0724-h6_VL - IMGT_CDR3	QQSNEDLLT
317	10-0724-h6_VL - IMGT_FR1	DIQLTQSPSSLSASVGDRATITCRAS
318	10-0724-h6_VL - IMGT_FR2	LHWYQQKPGKAPKLLIY
319	10-0724-h6_VL - IMGT_FR3	NVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC
320	10-0724-h6_VL - IMGT_FR4	FGQGTKLEIK

Table 4: Exemplary human immunoglobulin light chain constant regions, kappa (IGKC) and lambda 2 (IGLC2), and human immunoglobulin heavy chain constant region, gamma 1 (IGHG1), amino acid sequences of humanized P2RY8 antibodies

Seq ID NO.:	Name	Description	Sequence
321	Human Immunoglobulin kappa constant (IGKC)	Uniprot ID: P01834	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
322	human Immunoglobulin lambda constant 2 (IGLC2)	UniProt ID: P0DOY2	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
323	Human Immunoglobulin heavy constant gamma 1 (IGHG1)	Uniprot ID: P01857	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

Table 5: Exemplary nucleic acid sequences encoding mouse V_H and mouse V_L of chimeric P2RY8 antibodies

Seq ID NO.:	Name	Sequence
324	10-0690-m_VH	GATGTGCAGCTGCAGGAGAGCGGACCTGGACTGGTGAAGCC TAGCCAGAGCCTGAGCCTCACATGTATCGTGACCGGCTATAG CATCACCTCTGATTACGCCTGGAATTGGATCAGACAGTTTCCA GGCAACAAGCTGGAATGGATGGGCTACATCGACTACAGCGG CAGCACCTCCTACAACCCCAGCCTGAAAAGCAGAGTGTCCAT CACACGGGACACCAGCAAGAACCAGTTCTTCCTGCAACTGAA CAGCGTGACAACCGAGGACGCCGCTACATACTACTGCACCAG AGGCTTCTGGTACTTCGACGTGTGGGGCGCCGGCACCACCGT CACAGTGTCTTCT
325	10-0690-m_VL	GATATCGTGCTGACACAGTACCCCGCCTCTCTGGCCGTGTCCC TGGGCCAGCGGGCCACCATCAGCTGTAGAGCCTCCGAAAGC GTGGACAGCTACGGCTACACCTTTATGCACTGGTATCAGCAG AAACCTGGACAACCTCCAAAGCTGCTGATCTACCGGGCTTCTA ATCTGGAGAGCGGCATCCCTGCTAGATTCAGCGGATCTGGCA GCAGAACCGACTTCACCCTGACAATTAACCCCGTGGAAGCCG ACGACGTCGCCACATACTACTGCCAGCAGAGCAACGAGGATC CTTTCACCTTCGGCAGCGGCACCAAGCTGGAGATCAAG
326	10-0695-m_VH	GATGTGCAGCTGCAGGAGTCCGGACCTGGACTGGTGAAGCC TTCTCAGAGCCTGAGCCTCACCTGTACCGTCACAGGCTACAGC ATCACCTCTGATTACGCCTGGAATTGGATCAGACAGTTTCCAG GCAACAAGCTGGAATGGATGGGCTACATCTCTTATAGCGGCA GCACCTCCTACAACCCCAGCCTGAAAAGCAGAATCAGCATCA CACGGGACACCAGCAAGAACCAGTTCTTCCTGCAACTGAACA GCGTGACAACCGAGGACACAGCCACCTACTACTGCGCCAGAG GCTACTGGTACTTCGACGTGTGGGGCGCTGGCACCACCGTGA CAGTGTCCAGC
327	10-0695-m_VL	GATATCGTGCTGACACAGAGCCCTGCTTCTCTGGCCGTGTCCC TGGGCCAGCGGGCCACAATCAGCTGTAGAGCCTCCGAGAGC GTCGACAGCTACGGCTACAGCTTTATGCACTGGTACCAGCAG AAACCTGGCCAGCCTCCAAAGCTGCTGATCTACCGGGCCTCT AATCTGGAAAGCGGCATCCCCGCTAGATTCAGCGGCAGCGG ATCTAGAACCGACTTCACCCTGACCATCAACCCCGTGGAAGCC GACGACGTGGCCACCTACTACTGCCAGCAAAGCAACGAGGAT CCTTATACATTCGGCGGCGGAACCAAGCTGGAGATCAAG

328	10-0701-m_VH	GAGGTGCAGCTGCAGCAATCTGGCCCTGAGCTCGTGAAGCCT GGAGCTTCTATGAAGATCAGCTGTAAAGCCAGCAGCAGCAGC TTCACCGGCTACACCATGAACTGGGTCAAGCAGAGCCACGGC AAAAACCTGGAATGGATCGGCCTGATCAACCCATACAATGGC GGAACAACATACAACCAGAAGTTCAAGGGCAAGGCCACCCT GACCGTGGACAAGAGCAGCTCCACCGCCTACATGGAACTGCT GTCTCTGACATCCGAGGACAGCGCCGTGTACTACTGCGCCAG AGGCCGGGCTTATGTGAACCCCGGAGATTACGCCATGGACTA CTGGGGCCAGGGCACCAGCGTGACCGTGTCCAGC
329	10-0701-m_VL	CAAATCGTGCTGACACAGAGCCCTGCTATCATGAGCGCCTCTC TGGGCGAGAGAGTGACCATGACCTGTACCGCCAGCAGCTCTG CCTCCTCCAGCTACCTGCACTGGTACCAGCAGAAACCTGGCA GCTCCCCTAAGCTGTGGATCTACAGCACCAGCAACCTGGCCA GCGGCGTGCCCGCCAGATTCAGCGGAAGCGGCAGCGGCACC TCTTATAGCCTGACCATCCGGAGCATGGAAGCCGAGGACGCC GCTACATACTACTGCCACCAGTACCACAGATCTCCATACACCT TCGGCGGCGGAACAAAGCTGGAAATCAAG
330	10-0716-m_VH	GACGTGCACCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCC TAGCCAGAGCCTGAGCCTCACCTGTACCGTCACCGCCTACTCC ATCACCTCTGATTACGCCTGGAATTGGATCCGGCAGTTTCCAG GCAACAAGCTGGAATGGATGGGCTACGTGACCTACTCTGGCA CCACAACATACAACCCCTCTCTGAAAAGCAGAATCAGCATCAC AAGAGATACCAGCAAGAACCAGTTCTTCCTGCAACTGAACAG CGTGACCACCGAGGACACCGCTACATATTTCTGCGCCAGAGG CTACTGGTACTTCGACGTGTGGGGCGCCGGAACAACCGTGAC AGTGTCCAGC
331	10-0716-m_VL	GATATCGTGCTGACACAGAGCCCTGCTTCTCTGGCCGTGTCCC TGGGCCAGCGGGCCACCATCAGCTGTAGAGCCTCCGAGAGC GTCGACAGCTACGGCTACACCTTTATGCACTGGTATCAGCAG AAACCTGGCCAGCCTCCTAAGCTGCTGATCTACCGGGCCTCTA ATGTGCACAGCGGCATCCCAGCTAGATTCAGCGCCAGCGGAT CTAGAACCGACTTCACCCTGACCATTAACCCCGTGGAAGCCG ATGACATCGCCACATACTACTGCCAGCAAAGCAACGAGGACC CCTTCACATTCGGCAGCGGAACCAACCTGGAAATCAAG
332	10-0720-m_VH	GATGTGCAGTTTCAGGAGAGCGGACCTGGCCTGGTGAAGCC TAGCCAGAGCCAATCTCTGACCTGTACCGTCACCGGCTATAGC ATCACCTCTGATTACGCCTGGAATTGGCTGAGACAGTTCCCCG GCAACAAGCTGGAATGGATGGGCTACATCAGCTACAGCGGC ACCACAAACTACAACCCATCTCTGAAAAGCAGAATCTCCATCA CACGGGACACCAGCAAGAACCAGTTCTTCCTGCAGCTGAACA GCGTGACAAGCGAGGACACCGCCACATACTACTGCGCCAGA GGCTACTGGTACTTCGACGTGTGGGGAGCTGGCACAACCGT GACCGTGTCCTCC

333	10-0720-m_VL	GATATCGTGCTGACCCAGAGCCCTGCTTCCCTGGCCGTGTCCC TGGGCCAGCGGGCCACCATCAGCTGTAGAGCCAGCGAGAGA GTGGACAGCTACGGCTACACCTTTATGCACTGGTATCAGCAG AAACCTGGCCAGCCTCCAAAGCTGCTGATCTACCGGGCCTCT AATCTGGAAAGCGGCATCCCCGCTAGATTCAGCGGATCTGGC AGCAGAACCGACTTCACCCTGACAATTAACCCCGTGGAAGCC GACGACGTCGCCACATACTACTGCCAGCAAAGCAACGAGGAT CCTTTCACATTCGGCGGCGGAACCAAGCTGGAGATCAAG
334	10-0724-m_VH	GATGTGCAGCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCC TAGCCAGAGCCTGAGCCTGACATGTACCGTCACCGGATATTC TATCACAAGCGACTACGCCTGGAATTGGATCCGGCAGTTCCC CGGCAACAAGCTGGAATGGATGGGCTACATCACCTACAGCG GCACCACACGGTACAACCCAAGCCTGAAAAGCAGAATCAGCA TCACCAGAGATACCTCCAAGAACCACTTCTTCCTGCAACTGTC TTCTCTCACCACCGAGGACACCGCTACATACTACTGCGCCAGA GGCTTTTGGTACTTCGACGTGTGGGGCGCCGGCACAGCCGTG ACCGTGTCCAGC
335	10-0724-m_VL	GATATCGTGCTGACACAGAGCCCTGCTAGCCTGGCCGTGTCC CTGGGCCAGCGGGCCACAATTTCTTGTAGAGCCAGCGAGAGC GTCGACACCTACGGCTACAACTTCCTGCACTGGTATCAGCAG AAACCTGGCCAGCCTCCAAAGCTCCTGATCTACCGGGCCAGC AACCTGCAGAGCGGCATCCCCGCCAGATTCAGCGGATCTGGC AGCAGAGCTGATTTTACCCTGACCATCAACCCCGTGGAAGCC GACGACGTGGCCACATACTACTGCCAGCAATCCAATGAGGAC CTGCTGACCATCGGCGGAGGCACCAAGCTGGAAATCAAG
336	10-0725-m_VH	GATGTGCAGCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCC TAGCCAGAGCCTGAGCCTGACATGTACCGTCACCGGATATTC TATCACAAGCGACTACGCCTGGAATTGGATCCGGCAGTTCCC CGGCAACAAGCTGGAATGGATGGGCTACATCACCTACAGCG GCACCACACGGTACAACCCAAGCCTGAAAAGCAGAATCAGCA TCACCAGAGATACCTCCAAGAACCACTTCTTCCTGCAACTGTC TTCTCTCACCACCGAGGACACCGCTACATACTACTGCGCCAGA GGCTTTTGGTACTTCGACGTGTGGGGCGCCGGCACAGCCGTG ACCGTGTCCAGC
337	10-0725-m_VL	CAAGCCGTGGTGACACAGGAATCCGCCCTCACAACAAGCCCC GGCGAAACCGTGACCCTGACCTGTAGAAGCAGCACCGGCGC TGTGACCACCTCTAATTACGCCAACTGGGTCCAGGAGAAACC TGACCACCTGTTTACAGGCCTGATCGGCGGCACCAACAACCG GGCCCCTGGCGTGCCAGCCAGATTCAGCGGCTCTCTGATCGG AGATAAGGCCGCTCTGACCATCACCGGCGCCCAGACCGAGG ACGAGGCCATCTACTTCTGCGCCCTGTGGTACAGCAACCACT GGGTGTTCGGCGGAGGAACAAAGCTGACAGTGCTG

338	10-0728-m_VH	GAAGTGAAGCTTGAGGAGTCTGGAGGAGGCTTGGTGCAACC TGGAGGATCCATGAAACTCTCTTGTGCTGCCTCTGGATTCACT TTTAGTGACGCCTGGATGGACTGGGTCCGCCAGTCTCCAGAG AAGGGGCTTGAGTGGGTTGCTGAAATTAGAAGCAAAGCTAA TAATCATGCAACATACTATGCTGAGTCTGTGAAAGGGAGGTT CACCATCTCAAGAGATGATTCCAAAAGTAGTGTCTACCTGCAA ATGAACAGCTTAAGAGCTGAAGACACTGGCATTTATTACTGT ACGGGTTTTATGATTACGACGGCCTGGTTTGCTTACTGGGGC CAAGGGACTCTGGTCACTGTCTCGAGC
339	10-0728-m_VL	GAAAATGTGCTCACCCAGTCTCCAGCAATCATGTCTGCATCTC TAGGGGAGAAGGTCACCATGAGCTGCAGGGCCAGCTCAAGT GTAAATTACATGTACTGGTACCAGCAGAAGTCAGATGCCTCC CCCAAACTATGGATTTATTACACATCCAACCTGGCTCCTGGAG TCCCAGCTCGCTTCAGTGGCAGTGGGTCTGGGAACTCTTATTC TCTCACAATCAGCAGCATGGAGGGTGAAGATGCTGCCACTTA TTACTGCCAGCAGTTTACTAGTTCCCCGTACACGTTCGGAGGG GGGACCAAGCTGGAAATAAAA
340	10-0729-m_VH	GATGTGCAGCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCC CAGCCAGAGCCTGAGCCTGACCTGTACCGTGACCGGCTACAG CATCACAAGCGACTTCGCCTGGAACTGGATCCGGCAGGTGCC AGGCAACAAGCTGGAATGGATGGGCTATATCTCCTACTCTGG CACCACCAGATACAATCCTTTTCTGAAATCTAGAATCTCTATCA CCCGGGACACCAGCAAGAACCAGTTCTTCCTGCAACTCAACA GCGTGACCCCTGAGGATACCGCCACATACTACTGCGCCAGAG GCTACTGGTACTTCGACGTGTGGGGCGCTGGAACAACAGTCA CAGTGTCCAGC
341	10-0729-m_VL	GATATCGTGCTGACACAATCTCCAGCTAGCCTGGCCGTGTCCC TGGGCCAGCGGGCCACAATCAGCTGTAGAGCCAGCGAGAGC GTCGACAGCTACGGCTACACCTTTATGCACTGGTATCAGCACA AACCTGGCCAGTCCCCTAAGCTGCTGATCTACCGGGCCTCTAA TCTGGAAAGCGGCATCCCCGCTAGATTCAGCGGCAGCGGATC TAGAACCGACTTCACCCTGACCATCAACCCCGTGGAAGCCGA CGACGTGGCCACCTACTACTGCCAGCAGAGCAACGACGATCC TTACACCTTCGGCGGCGGAACACAGCTGGAGGTGAAG

Table 6: Exemplary nucleic acid sequence encoding humanized V_H and humanized V_L of humanized P2RY8 antibodies

Seq ID NO.:	Name	Sequence

342	10-0716-h1_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGGTGAGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGTTCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGAT GAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
343	10-0716-h1_VL	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
344	10-0716-h2_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGGTGAGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGTTCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGAT GAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
345	10-0716-h2_VL	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCATCCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCGTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
346	10-0716-h3_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC

347	10-0716-h3_VL	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
348	10-0716-h4_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
349	10-0716-h4_VL	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCATCCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCGTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
350	10-0716-h5_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
351	10-0716-h5_VL	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCAGGACCGACTTCACCCTGACCATCAGCAGCCTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG

352	10-0716-h6_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
353	10-0716-h6_VL	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCATCCCCAGCAGGTTCAGCGGCAGC GGCAGCAGGACCGACTTCACCCTGACCATCAGCAGCGTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
354	10-0716-h8_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACGCCGACAGCCTGAAGGGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
355	10-0716-h8_VL	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAG CGTGGACAGCTACGGCTACACCTTCATGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
356	10-0724-h3_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTTCTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC

357	10-0724-h3_VL	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAG CGTGGACACCTACGGCTACAACTTCCTGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCTGCTGACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
358	10-0724-h4_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTTCTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
359	10-0724-h4_VL	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAG CGTGGACACCTACGGCTACAACTTCCTGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGCAGAGCGGCATCCCCAGCAGGTTCAGCGGCAGC GGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCGTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCTGCTGACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
360	10-0724-h5_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTTCTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
361	10-0724-h5_VL	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAG CGTGGACACCTACGGCTACAACTTCCTGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGC GGCAGCAGGACCGACTTCACCCTGACCATCAGCAGCCTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCTGCTGACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG

362	10-0724-h6_VH	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGC CCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTAC AGCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAG CGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCAC CATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCT GAACAGCGTGAGGGCCGAGGACACCGCCGTGTACTACTGCG CCAGGGGCTTCTGGTACTTCGACGTGTGGGGCCAGGGCACC ACCGTGACCGTGAGCAGC
363	10-0724-h6_VL	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGC GTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAG CGTGGACACCTACGGCTACAACTTCCTGCACTGGTACCAGCA GAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCA GCAACGTGCAGAGCGGCATCCCCAGCAGGTTCAGCGGCAGC GGCAGCAGGACCGACTTCACCCTGACCATCAGCAGCGTGCAG CCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAACGAG GACCTGCTGACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 7: Exemplary nucleic acid sequence encoding human immunoglobulin light chain constant regions, kappa (IGKC) and lambda 2 (IGLC2), and human immunoglobulin heavy chain constant region, gamma 1 (IGHG1), of humanized P2RY8 antibodies

Seq ID NO.:	Name	Description	Sequence
364	Human Immunoglobulin kappa constant (IGKC)	for Uniprot ID: P01834	CGTACGGTGGCGGCGCCATCTGTCTTCATCTTCCC GCCATCTGATGAGCAGTTGAAATCTGGAACTGCCT CTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGA GAGGCCAAAGTACAGTGGAAGGTGGATAACGCCC TCCAATCGGGTAACTCCCAGGAGAGTGTCACAGA GCAGGACAGCAAGGACAGCACCTACAGCCTCAGC AGCACCCTGACGCTGAGCAAAGCAGACTACGAGA AACACAAAGTCTACGCCTGCGAAGTCACCCATCAG GGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAG GGGAGAGTGTTAG
365	human Immunoglobulin lambda constant 2 (IGLC2)	for UniProt ID: P0DOY2	GGTCAGCCCAAGGCGGCGCCCTCGGTCACTCTGTT CCCGCCCTCCTCTGAGGAGCTTCAAGCCAACAAGG CCACACTGGTGTGTCTCATAAGTGACTTCTACCCG GGAGCCGTGACAGTGGCCTGGAAGGCAGATAGCA GCCCCGTCAAGGCGGGAGTGGAGACAACCACACC CTCCAAACAAAGCAACAACAAGTACGCGGCCAGC AGCTATCTGAGCCTGACGCCTGAGCAGTGGAAGT CCCACAGAAGCTACAGCTGCCAGGTCACGCATGA

			AGGGAGCACCGTGGAGAAGACAGTGGCCCCTACA GAATGTTCATAG
366	Human Immunoglobulin heavy constant gamma 1 (IGHG1)	for Uniprot ID: P01857	GCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGC ACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCG GCCCTGGGCTGCCTGGTCAAGGACTACTTCCCCGA ACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTG ACCAGCGGCGTGCACACCTTCCCGGCTGTCCTACA GTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGA CCGTGCCCTCCAGCAGCTTGGGCACCCAGACCTAC ATCTGCAACGTGAATCACAAGCCCAGCAACACCAA GGTGGACAAGAAAGTTGAGCCCAAATCTTGTGAC AAAACTCACACATGCCCACCGTGCCCAGCACCTGA ACTCCTGGGGGGACCGTCAGTCTTCCTCTTCCCCCC AAAACCCAAGGACACCCTCATGATCTCCCGGACCC CTGAGGTCACATGCGTGGTGGTGGACGTGAGCCA CGAAGACCCTGAGGTCAAGTTCAACTGGTACGTG GACGGCGTGGAGGTGCATAATGCCAAGACAAAGC CGCGGGAGGAGCAGTACAACAGCACGTACCGTGT GGTCAGCGTCCTCACCGTCCTGCACCAGGACTGGC TGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAA CAAAGCCCTCCCAGCCCCCATCGAGAAAACCATCT CCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGT GTACACCCTGCCCCCATCCCGGGATGAGCTGACCA AGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGG CTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGAACAACTACAAGACCA CGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCC TCTACAGCAAGCTCACCGTGGACAAGAGCAGGTG GCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGC ATGAGGCTCTGCACAACCACTACACGCAGAAGAG CCTCTCCCTGTCTCCGGGTAAATGA

Table 8: Exemplary amino acid sequence of mGFP marker or mycDDK epitope tag

Seq ID NO.:	Name	Sequence
367	mGFP	MSGGEELFAGIVPVLIELDGDVHGHKFSVRGEGEGDADYGKLEIKFICTTGKLPV PWPTLVTTLCYGIQCFARYPEHMKMNDFFKSAMPEGYIQERTIQFQDDGKYKT RGEVKFEGDTLVNRIELKGKDFKEDGNILGHKLEYSFNSHNVYIRPDKANNGLEA

		NFKTRHNIEGGGVQLADHYQTNVPLGDGPVLIPINHYLSTQTKISKDRNEARDH MVLLESFSACCHTHGMDELYR
368	mycDDK	EQKLISEEDLAANDILDYKDDDDKV

Table 9: Exemplary amino acid sequence of P2RY8 proteins

Seq ID NO.:	Name	Sequence
369	Human P2RY8 protein (UniProt ID: Q86VZ1)	MQVPNSTGPDNATLQMLRNPAIAVALPVVYSLVAAVSIPGNLFSLWVL CRRMGPRSPSVIFMINLSVTDLMLASVLPFQIYYHCNRHHWVFGVLLC NVVTVAFYANMYSSILTMTCISVERFLGVLYPLSSKRWRRRRYAVAACA GTWLLLLTALSPLARTDLTYPVHALGIITCFDVLKWTMLPSVAMWAVFL FTIFILLFLIPFVITVACYTATILKLLRTEEAHGREQRRRAVGLAAVVLLAFV TCFAPNNFVLLAHIVSRLFYGKSYYHVYKLTLCLSCLNNCLDPFVYYFASR EFQLRLREYLGCRRVPRDTLDTRRESLFSARTTSVRSEAGAHPEGMEGA TRPGLQRQESVF
370	*Macaca fascicularis* P2RY8 protein (NCBI RefSeq: XP_005595888)	MEETGSSLPTHVPTLLGPRGALPAATSPPAPLSRAPFPLQSPGEDPSRM HVPNSTGPDNATLQMLRNPTIAVALPVVYSLVALVSIPGNLFSLWVLCR RIGPKSPSVIFMINLSVTDLMLASVLPFQIYYHCNRNHWVFGVLLCNVVT VAFYANMYSSILTMTCISVERFLGVLYPLSSTRWRRRRYAVAACAGTWL LLLAALSPLARTDLTYPVHALGIVTCFDVLKWTMLPSVAMWAVFLFTIFI LLFLIPFVVTVACYTATILKLLRTEEAHGREQRRRAVGLAVVVLLAFVTCF APNNFVLLAHIVGRLFYGKSYYHVYKLTLCLSCLNNCLDPFVYYFASREFQ LRLREYLGCRQVPGDPLDTRRESLFSARTTSMRSEAGAHPEGLEGAPRP GLMRQESEF
371	dog P2RY8 protein (NCBI RefSeq: XP_013967130)	MDMNVSGPDNATILMLRDPVIAVALPVVYSLVAVVSIPGNLFSLWVLC RHIGPKSPSVVFMINLSVTDLMLASVLPFQIYYHRNGNHWVFGEVLCN VVTVVFYANMYSSILTMTCISVERFLGVVYPLASAPWRRRRYAVAACAA AWLLLLVALSPLARTDLTYAVEELGIVTCFDVLKSTMLPSVAMWAIFLFT LFIVLFFIPFVVTVACYTATILTLLRASDPQGRGQRRRAVSLAFVVLLAFVT CFAPNNFVLLVHMVSRLFLGRSYYHVYKLTLCLSCVNNCLDPFVYYFASR EFQLRLRRYLGYGPLPATCRDAGRDSLFSPRTLSARSMSSGHGDGLEAP GRPALRRQESVF

Table 10: Six-humanized P2RY8 antibodies - Flow by iQUE using native positive cell lines

Median AF647 (RL1-H) of singlets	1µg Ab/reaction (20µg Ab/ml)				
	KARPAS-1106P (P2RY8+)	SU-DHL-5 (P2RY8+)	SU-DHL-10 (P2RY8+)	SCC-3 (P2RY8-)	M202 (P2RY8-)
P2RY8mAb-716-h1	140,210.0	70,015.5	41,161.0	2,647.0	6,580.0
P2RY8mAb-716-h2	154,985.0	87,609.0	44,179.5	2,121.0	6,059.0
P2RY8mAb-716-h3	180,562.5	108,609.0	54,995.0	2,994.0	8,640.5
P2RY8mAb-716-h4	179,088.0	120,538.0	58,411.5	3,239.0	7,963.0
P2RY8mAb-716-h5	189,148.0	151,461.0	51,869.0	3,188.5	7,874.0
P2RY8mAb-716-h6	187,806.5	157,880.0	60,388.0	3,070.0	8,032.0
P2RY8mAb-716	148,410.5	103,176.0	46,205.0	2,195.0	3,146.0
2nd Ab only	1,910.0	2,548.0	3,178.0	2,028.0	3,237.0
Median AF647 (RL1-H) of singlets	0.3µg Ab/reaction (6µg Ab/ml)				
	KARPAS-1106P (P2RY8+)	SU-DHL-5 (P2RY8+)	SU-DHL-10 (P2RY8+)	SCC-3 (P2RY8-)	M202 (P2RY8-)
P2RY8mAb-716-h1	95,365.5	52,038.0	31,972.0	2,570.0	4,066.0
P2RY8mAb-716-h2	107,938.0	69,308.0	35,092.5	2,170.0	4,140.0
P2RY8mAb-716-h3	114,222.0	79,132.5	38,445.5	2,691.0	5,412.0
P2RY8mAb-716-h4	91,639.0	88,167.0	36,863.0	2,876.5	5,086.0
P2RY8mAb-716-h5	94,406.0	116,132.5	37,082.5	2,684.0	5,241.5
P2RY8mAb-716-h6	114,619.0	120,156.5	40,248.0	2,869.0	5,459.0
P2RY8mAb-716	86,245.0	72,675.5	26,580.0	2,741.0	2,861.0
2nd Ab only	2,270.0	2,401.0	2,803.0	2,028.0	3,233.0

Table 10 shows binding activity of six humanized anti-P2RY8 antibodies (716-h1 (also referred to herein as 10-0716-h1, P2RY8 mAb-716-h1, P2RY8mAb-716-h1 or P2RY8hAb 0716-h1), 716-h2 (also referred to herein as 10-0716-h2, P2RY8 mAb-716-h2, P2RY8mAb-716-h2 or P2RY8hAb 0716-h2), 716-h3 (also referred to herein as 10-0716-h3, P2RY8 mAb-716-h3, P2RY8mAb-716-h3 or P2RY8hAb 0716-h3), 716-h4 (also referred to herein as 10-0716-h4, P2RY8 mAb-716-h4, P2RY8mAb-716-h4 or P2RY8hAb 0716-h4), 716-h5 (also referred to herein as 10-0716-h5, P2RY8 mAb-716-h5,

P2RY8mAb-716-h5 or P2RY8hAb 0716-h5), or 716-h6 (also referred to herein as 10-0716-h6, P2RY8 mAb-716-h6, P2RY8mAb-716-h6 or P2RY8hAb 0716-h6)) or a chimeric anti-P2RY8 antibody, 716-m (also referred to herein as P2RY8 mAb-716 and 716-m (hIgG1), wherein mouse heavy and light chain constant region are replaced with human IgG1-kappa antibody constant region, to a panel of native human cancer cell lines positive for human P2RY8 receptor: human large B-cell lymphoma cell line, Karpas-1106P (RRID: CVCL_1821), human large B-cell lymphoma cell line, SU-DHL-5 (ATCC CRL-2958) and human B cell lymphoma cell line, SU-DHL-10 (ATCC CRL-2963); or negative for P2RY8 receptor: human B-cell non-Hodgkin lymphoma cell line, SCC-3 (RRID: CVCL_1683) and human melanoma cell line, M202 (RRID: CVCL_D746). Antibody bound cells were detected using a secondary antibody, mouse anti-human IgG-Fc conjugated to Alexa Fluor® 647 fluorescent dye (Biolegend, San Diego; Catalog #: 409320, Clone HP6017), and fluorescence was measured on a flow cytometer (Intellicyt iQue® Advanced Flow Cytometer platform). Median AF647 fluorescence from two different primary antibody concentrations are reported.

Table 11: Six humanized P2RY8 antibodies - Flow by iQUE using overexpressing (OE) positive cell lines

Median AF647 (RL1-H) of singlets	1µg Ab/reaction (20µg Ab/ml)		0.3µg Ab/reaction (6µg Ab/ml)	
	HEK293T Parental	HEK293T P2RY8mGFP Clone 5	HEK293T Parental	HEK293T P2RY8mGFP Clone 5
P2RY8mAb-716-h1	4,486.0	1,391,908.0	3,500.0	1,221,390.0
P2RY8mAb-716-h2	4,216.0	1,526,965.0	3,408.0	1,311,726.5
P2RY8mAb-716-h3	6,021.0	1,797,667.0	4,120.0	1,337,735.5
P2RY8mAb-716-h4	5,999.0	1,607,155.0	4,242.0	1,267,115.0
P2RY8mAb-716-h5	5,404.0	1,725,099.0	3,807.0	1,515,889.0
P2RY8mAb-716-h6	6,164.0	1,933,399.5	4,254.0	1,473,938.0
P2RY8mAb-716	2,507.0	1,751,169.0	3,439.0	1,342,010.0
2nd Ab only	3,102.0	4,319.0	3,311.0	4,815.0
GFP Signal	1µg Ab/reaction (20µg Ab/ml)		0.3µg Ab/reaction (6µg Ab/ml)	
	HEK293T Parental		HEK293T Parental	

		HEK293T P2RY8mGFP Clone 5		HEK293T P2RY8mGFP Clone 5
P2RY8mAb-716-h1	6,616.0	1,328,562.0	6,581.0	1,408,202.0
P2RY8mAb-716-h2	6,693.0	1,309,788.0	6,594.5	1,356,408.5
P2RY8mAb-716-h3	6,282.0	1,374,796.5	6,476.0	1,341,091.0
P2RY8mAb-716-h4	6,583.0	1,326,720.0	6,482.0	1,338,132.0
P2RY8mAb-716-h5	6,561.0	1,318,198.0	6,349.0	1,414,913.0
P2RY8mAb-716-h6	6,458.0	1,384,449.0	6,645.5	1,342,186.5
P2RY8mAb-716	6,369.0	1,336,354.0	6,540.0	1,414,220.0
2nd Ab only	6,423.5	1,320,631.5	6,460.0	1,393,984.5

Table 11 shows binding activity of the six humanized anti-P2RY8 antibodies and a chimeric mouse-human anti-P2RY8 antibody as described in Table 10 measured on a human embryonic kidney cell line, HEK293T, or HEK293T P2RY8mGFP clone 5 cell line, a stable HEK293T cell line overexpressing human P2RY8 receptor-mGFP fusion protein (as provided in Table 39). Top half of table, AF647 fluorescence determined at two different primary antibody concentrations; bottom half of table, GFP fluorescence.

Table 12: KD for P2RY8 hAbs by KinExA 4000 - HEK293T P2RY8 mGFP Clone 5 cells

Antibody Name	KD (nM)		
	KD (nM)	Error%	95% Confidence Interval (CI)
P2RY8mAb-716-h3	**5.46**	2.11	4.15nM - 7.15nM
P2RY8mAb-716-h4	**5.49**	3.34	3.59nM - 8.41nM
P2RY8mAb-716-h5	**5.51**	5.46	2.69nM - 11.68nM
P2RY8mAb-716-h6	**4.25**	2.83	2.89nM - 6.10nM
P2RY8mAb-716	**38.43**	2.21	13.06nM - 94.60nM

Antibody Name	Expression Level		Equilibrium Curves
	Expression Level	95% Confidence Interval (CI)	
P2RY8mAb-716-h3	1.709E+06	1.374E+06 - 2.104E+06	500pM, 50nM
P2RY8mAb-716-h4	2.391E+06	1.774E+06 - 3.262E+06	500pM, 50nM

P2RY8mAb-716-h5	2.829E+06	1.756E+06 - 5.164E+06	500pM, 50nM
P2RY8mAb-716-h6	1.477E+06	1.069E+06 - 1.971E+06	500pM, 50nM
P2RY8mAb-716	4.744E+05	1.061E+05 - 1.327E+06	500pM, 50nM

Antibody Name	Cell Model	Cells were Detached by
P2RY8mAb-716-h3	HEK293T P2RY8mGFP Clone 5	Versene®
P2RY8mAb-716-h4	HEK293T P2RY8mGFP Clone 5	Versene®
P2RY8mAb-716-h5	HEK293T P2RY8mGFP Clone 5	Versene®
P2RY8mAb-716-h6	HEK293T P2RY8mGFP Clone 5	Versene®
P2RY8mAb-716	HEK293T P2RY8mGFP mass pop	Versene®

Table 12 summarizes dissociation constant, K_D, determined for four humanized anti-P2RY8 antibodies (10-0716-h3 (also referred to herein as P2RY8 mAb-716-h3), 10-0716-h4 (also referred to herein as P2RY8 mAb-716-h4), 10-0716-h5 (also referred to herein as P2RY8 mAb-716-h5), or 10-0716-h6 (also referred to herein as P2RY8 mAb-716-h6)) or chimeric anti-P2RY8 antibody (10-0716-m (also referred to herein as P2RY8 mAb-716, 0716m)) binding to HEK293T cells stably overexpressing a human P2RY8-mGFP fusion protein (HEK293T P2RY8mGFP Clone 5) or transiently transfected with a human P2RY8-mGFP fusion protein (HEK293T P2RY8mGFP mass pop).

Table 13: Tox model flow test: read by BD Accuri C6

FL4H/P2RY8 signal	716-h3 4ug/ml	anti-human secondary only	no antibody
HEK293T parental	875.87	663.36	698.62
HEK293T human P2RY8 mGFP Clone5	47,856.28	1,499.03	1,765.90
610-HEK293T macP2RY8 mGFP mass pop	99,535.48	1,125.80	1,107.93

618-HEK293T dogP2RY8 mGFP mass pop	3,080.36	1,869.72	1,094.42
FL1H/GFP signal	716-h3 4ug/ml	anti-human secondary only	no antibody
HEK293T parental	2,469.79	2,452.07	2,762.44
HEK293T human P2RY8 mGFP Clone5	180,915.82	173,545.15	210,959.58
610-HEK293T macP2RY8 mGFP mass pop	239,566.01	229,551.88	266,772.35
618-HEK293T dogP2RY8 mGFP mass pop	1,568,850.50	1,507,115.05	1,746,297.81

Table 13 shows flow cytometry assessment of the binding activity of a humanized anti-P2RY8 antibody, P2RY8 mAb-716-h3, to HEK293 cells overexpressing mGFP fluorescent fusion protein (Table 8; SEQ ID NO: 367 for mGFP protein sequence; also, see Table 39 for fusion protein) to human P2RY8 (UniProt accession number: Q86VZ1; SEQ ID NO: 369), monkey P2RY8 (NCBI RefSeq accession number: XP_005595888.1; SEQ ID NO: 370), or dog P2RY8 (NCBI RefSeq accession number: XP_013967130.1; SEQ ID NO: 371). Top half of table – P2RY8 signal from fluorescently labeled secondary antibody detection of anti-P2RY8 antibody bound to cell; bottom half of table – GFP signal.

The following shows the descriptions of Tables 14-39.

[00248] **Table 14** shows amino acid sequences of mouse heavy chain variable region (V_H) and light chain variable region (V_L) of two chimeric anti-P2RY8 antibodies, 10-0690-m and 10-0695-m, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by ImMunoGeneTics (IMGT) method.

[00249] **Table 15** shows amino acid sequences of mouse heavy chain variable region (V_H) and light chain variable region (V_L) of two chimeric anti-P2RY8 antibodies, 10-0701-m and 10-0716-m, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00250] **Table 16** shows amino acid sequences of mouse heavy chain variable region (V_H) and light chain variable region (V_L) of two chimeric anti-P2RY8 antibodies, 10-0720-m and 10-0724-m, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00251] **Table 17** shows amino acid sequences of mouse heavy chain variable region (V_H) and light chain variable region (V_L) of two chimeric anti-P2RY8 antibodies, 10-0725-m and 10-0728-m, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00252] **Table 18** shows amino acid sequences of mouse heavy chain variable region (V_H) and light chain variable region (V_L) of a chimeric anti-P2RY8 antibody, 10-0729-m, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00253] **Table 19** shows amino acid sequences of humanized heavy chain variable region (V_H) and light chain variable region (V_L) of two humanized anti-P2RY8 antibodies, 10-0716-h1 and 10-0716-h2, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00254] **Table 20** shows amino acid sequences of humanized heavy chain variable region (V_H) and light chain variable region (V_L) of two humanized anti-P2RY8 antibodies, 10-0716-h3 and 10-0716-h4, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00255] **Table 21** shows amino acid sequences of humanized heavy chain variable region (V_H) and light chain variable region (V_L) of two humanized anti-P2RY8 antibodies, 10-0716-h5 and 10-0716-h6, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00256] **Table 22** shows amino acid sequences of humanized heavy chain variable region (V_H) and light chain variable region (V_L) of two humanized anti-P2RY8 antibodies, 10-0716-h8 and 10-0724-h3, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00257] **Table 23** shows amino acid sequences of humanized heavy chain variable region (V_H) and light chain variable region (V_L) of two humanized anti-P2RY8 antibodies, 10-0724-h4 and 10-0724-h5, along with the lengths, positions and amino

acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00258] **Table 24** shows amino acid sequences of humanized heavy chain variable region (V_H) and light chain variable region (V_L) of a humanized anti-P2RY8 antibody, 10-0724-h6, along with the lengths, positions and amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method.

[00259] **Table 25** shows amino acid sequences of mouse heavy chain variable region (V_H) and mouse light chain variable region (V_L) of three chimeric anti-P2RY8 antibodies, 10-0690-m, 10-0695-m and 10-0701-m, along with the amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by ImMunoGeneTics (IMGT) method and the name of the expression vector producing the antibody.

[00260] **Table 26** shows amino acid sequences of mouse heavy chain variable region (V_H) and mouse light chain variable region (V_L) of three chimeric anti-P2RY8 antibodies, 10-0716-m, 10-0720-m and 10-0724-m, along with the amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method and the name of the expression vector producing the antibody.

[00261] **Table 27** shows amino acid sequences of mouse heavy chain variable region (V_H) and mouse light chain variable region (V_L) of three chimeric anti-P2RY8 antibodies, 10-0725-m, 10-0728-m and 10-0729-m, along with the amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method and the name of the expression vector producing the antibody.

[00262] **Table 28** shows amino acid sequences of heavy chain variable region (V_H) and light chain variable region (V_L) of three humanized anti-P2RY8 antibodies, 10-0716-h1, 10-0716-h2 and 10-0716-h3, along with the amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method and the name of the expression vector producing the antibody.

[00263] **Table 29** shows amino acid sequences of heavy chain variable region (V_H) and light chain variable region (V_L) of three humanized anti-P2RY8 antibodies, 10-0716-h4, 10-0716-h5 and 10-0716-h6, along with the amino acid sequences of the

complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method and the name of the expression vector producing the antibody.

[00264] **Table 30** shows amino acid sequences of heavy chain variable region (V_H) and light chain variable region (V_L) of three humanized anti-P2RY8 antibodies, 10-0716-h8, 10-0724-h3 and 10-0724-h4, along with the amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method and the name of the expression vector producing the antibody.

[00265] **Table 31** shows amino acid sequences of heavy chain variable region (V_H) and light chain variable region (V_L) of two humanized anti-P2RY8 antibodies, 10-0724-h5 and 10-0724-h6, along with the amino acid sequences of the complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method and the name of the expression vector producing the antibody.

[00266] **Table 32** shows amino acid sequences of the human immunoglobulin light chain, kappa, constant region (IGKC; UniProt ID: P01834), human immunoglobulin light chain, lambda, constant 2 region (IGLC2; UniProt ID: P0DOY2), and human immunoglobulin heavy chain constant region gamma 1 (IGHG1; UniProt ID: P01857) in some embodiments of the humanized anti-P2RY8 antibodies of the invention.

[00267] **Table 33** shows nucleic acid sequences encoding mouse heavy chain variable region (V_H) and mouse light chain variable region (V_L) for nine chimeric anti-P2RY8 antibodies, 10-0690-m, 10-0695-m, 10-0701-m, 10-0716-m, 10-0720-m, 10-724-m, 10-0725-m, 10-0728-m and 10-0729-m.

[00268] **Table 34** shows nucleic acid sequences encoding humanized heavy chain variable region (V_H) and humanized light chain variable region (V_L) for eleven humanized anti-P2RY8 antibodies, 10-0716-h1, 10-0716-h2, 10-0716-h3, 10-0716-h4, 10-0716-h5, 10-0716-h6, 10-0716-h8, 10-0724-h3, 10-724-h4, 10-0724-h5, and 10-0724-h6.

[00269] **Table 35** shows nucleic acid sequences encoding the human immunoglobulin light chain, kappa, constant region (IGKC), human immunoglobulin light chain, lambda, constant region 2 (IGLC2), and human immunoglobulin heavy chain constant region gamma 1 (IGHG1) used in some embodiments of the invention to produce full length humanized anti-P2RY8 antibody.

[00270] **Table 36** shows nucleic acid sequences encoding CDRs of heavy and light chain variable regions of chimeric anti-P2RY8 antibodies, 10-0690-m, 10-0695-m, 10-0701-m, 10-0716-m, 10-0720-m, 10-0724-m, 10-0725-m, 10-0728-m, and 10-0729-m.

[00271] **Table 37** shows nucleic acid sequences encoding heavy chain variable region (V_H), light chain variable region (V_L), complementary determining regions (CDRs) and framework regions (FRs) as defined by IMGT method of humanized anti-P2RY8 antibodies of 10-0716-m (10-0716-h1, 10-0716-h2, 10-0716-h3, 10-0716-h4, 10-0716-h5, 10-0716-h6 and 10-0716-h8) and 10-0724-m (10-0724-h3, 10-0724-h4, 10-0724-h5, and 10-0724-h6).

[00272] **Table 38** shows amino acid sequences of human P2RY8 protein (UniProt ID: Q86VZ1; SEQ ID NO: 369), crab-eating macaque (*Macaca fascicularis*) P2RY8 protein (NCBI Ref Seq: XP_005595888; SEQ ID NO: 370), and dog P2RY8 protein (NCBI Ref Seq: XP_013967130; SEQ ID NO: 371).

[00273] **Table 39** shows amino acid sequences of P2RY8 fusion protein of human P2RY8 protein (UniProt ID: Q86VZ1; SEQ ID NO: 369), crab-eating macaque (*Macaca fascicularis*) P2RY8 protein (NCBI Ref Seq: XP_005595888; SEQ ID NO: 370), or dog P2RY8 protein (NCBI Ref Seq: XP_013967130; SEQ ID NO: 371) and a fluorescent protein (mGFP; SEQ ID NO: 367) expressed in transfected cells.

Table 14: Mouse V_H, V_L, CDR and FR sequences from chimeric anti-P2RY8 antibodies, 10-0690-m and 10-0695-m

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0690-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0690-m_VH	IMGT	Sequence Fragment	DVQLQESGPGLVKPSQS LSLTCTVT	GYSITSDY A	WNWIRQFPGNKLEWMGY ISYSGST	EPSGST	SYNPSLKSRISITRDTSKN QFFLQLNSVTTEDTATYYC	TRGPWYFD V	WGAGTTVTVSS	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYA WNWIRQFPGNKLEWMGYISYSGSTSYNPSLKS RISITRDTSKNQFFLQLNSVTTEDTATYYCTRGP WYFDVWGAGTTVTVSS	10-0690-m_VH
10-0690-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0690-m_VH
10-0690-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0690-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0690-m_VL	IMGT	Sequence Fragment	DIVLTQSPASLAVSLGQR ATISCRAS	ESVDSYG YSF	LMHWYQQKPGQPPKLLIY	RAS	NLESGIPARFSGSGSRTDF TLTINPVEADDVATYYC	QQSNEDPYT	FGGGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYSF LMHWYQQKPGQPPKLLIYRASNLESGIPARFSG SGSRTDFTLTINPVEADDVATYYCQQSNEDPYTF GGGTKLEIK	10-0690-m_VL
10-0690-m_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0690-m_VL
10-0690-m_VL	IMGT	Length	26	10	17	3	36	9	10		10-0690-m_VL

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0695-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0695-m_VH	IMGT	Sequence Fragment	DVQLQESGPGLVKPSQS LSLTCTVT	GYSITSDY A	WNWIRQFPGNKLEWMGY ISYSGST	EPSGST	SYNPSLKSRISITRDTSKNQ FFLQLNSVTTEDTATYYC	ARGPWYFD V	WGAGTTVTVSS	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYA WNWIRQFPGNKLEWMGYISYSGSTSYNPSLKS RISITRDTSKNQFFLQLNSVTTEDTATYYCARGP WYFDVWGAGTTVTVSS	10-0695-m_VH
10-0695-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0695-m_VH
10-0695-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0695-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0695-m_VL	IMGT	Sequence Fragment	DIVLTQSPASLAVSLGQR ATISCRAS	ESVDSYG YSF	LMHWYQQKPGQPPKLLIY	RAS	NLESGIPARFSGSGSRTDF TLTINPVEADDVATYYC	QQSNEDPYT	FGGGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYSF LMHWYQQKPGQPPKLLIYRASNLESGIPARFSG SGSRTDFTLTINPVEADDVATYYCQQSNEDPYTF GGGTKLEIK	10-0695-m_VL
10-0695-m_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57-92	93 - 101	102 - 111		10-0695-m_VL
10-0695-m_VL	IMGT	Length	26	10	17	3	36	9	10		10-0695-m_VL

Table 15: Mouse V_H, V_L, CDR and FR sequences from chimeric anti-P2RY8 antibodies, 10-0701-m and 10-0716-m

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0701-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0701-m_VH	IMGT	Sequence Fragment	EVQLQQSGPELVKPGASMKISCKASSS	SSFTGYT	MNWVKQSHGK NLEWIGL	INPYNGG T	TYNQKFKGKATLTVDKSS STAYMELLSITSEDSAVYY C	ARGRAYNPG DYAMDY	WGQGTSVTVSS	EVQLQQSGPELVKPGASMKISCKASSS FTGYTMNWVKQSHGKNLEWIGLINPY NGGTTYNQKFKGKATLTVDKSSTAYM ELLSITSEDSAVYYCARGRAYNPGDYA MDYWGQGTSVTVSS	10-0701-m_VH
10-0701-m_VH	IMGT	Residues	1 - 25	26 - 33	34 - 50	51 - 58	59 - 96	97 - 112	113 - 123		10-0701-m_VH
10-0701-m_VH	IMGT	Length	25	8	17	8	38	16	11		10-0701-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0701-m_VL	IMGT	Sequence Fragment	QIVLTQSPAIMSASLGE RVTMTCTAS	SSASSSY	LHWYQQKPGSS PKLWIY	STS	RLASGVPARFSGSGSGTS YSLTISRMEAEDAATYYC	HQYHKSPYT	FGGGTKLEIK	QIVLTQSPAIMSASLGERVTMTCTASS ASSSYLHWYQQKPGSSPKLWIYSTSNLA SGVPARFSGSGSGTSYSLTISRMEAEDA ATYYCHQYHKSPYTFGGGTKLEIK	10-0701-m_VL
10-0701-m_VL	IMGT	Residues	1 - 26	27 - 33	34 - 50	51 - 53	54-89	90 - 98	99 - 108		10-0701-m_VL
10-0701-m_VL	IMGT	Length	26	7	17	3	36	9	10		10-0701-m_VL

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0716-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-m_VH	IMGT	Sequence Fragment	DVHLQESGPGLVKPSDSLSLTCTVTGYS ISDYAWNWIRQFPGNKLEWMGYVTY SGTTYNPSLKSRISITRDTSKNQFFLQL MSVTTEDTATYFCARGWYFDVWGAG TTVTVSS	WGAGTTVTVSS	ARGWYFDV		TYNPSLKSRISITRDTSKN QFFLQLNSVTTEDTATYF C				
10-0716-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-m_VH
10-0716-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-m_VL	IMGT	Sequence Fragment	DIVLTQSPASLAVSLGQRATISCRASES VDSYGYSFMHWYQQKPGQPPKLLIY FASNLES GIPARFSASGSGTDFTLTINPVEA EDVATYYCQQSNEDPFTFGSGTNLEIK	VDSYGYSFMH	WYQQKPGQPPKLLIY	RAS	NLESGIPARFSASGSGTD FTLTINPVEAEDVATYYC	QQSNEDPFT	FGSGTNLEIK	DIVLTQSPASLAVSLGQRATISCRASESV DSYGYSFMHWYQQKPGQPPKLLIYRAS NLESGIPARFSASGSGTDFTLTINPVEA EDVATYYCQQSNEDPFTFGSGTNLEIK	10-0716-m_VL
10-0716-m_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57-92	93 - 101	102 - 111		10-0716-m_VL
10-0716-m_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-m_VL

Table 16: Mouse V_H, V_L, CDR and FR sequences from chimeric anti-P2RY8 antibodies, 10-0720-m and 10-0724-m

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0720-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0720-m_VH	IMGT	Sequence Fragment	DVQLQESGPGLVKPSQSLSLTCTVTGY SISDYAWNWIRQFPGNKLEWMGYIS	GYSITSDY A	WNWIRQFPGNK LEWMGY	ISYSGTT	RYNPSLKSRISITRDTSKN QFFLQLNSVTSEDTATYY C	ARGYWYFDV	WGSAGTTVTVSS	DVQLQESGPGLVKPSQSLSLTCTVTGY SITSDYAWNWIRQFPGNKLEWMGYIS YSGTTNYNPSLKSRISITRDTSKNQFFLQ LNSVTSEDTATYYCARGYWYFDVWGA GTTVTVSS	10-0720-m_VH
10-0720-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0720-m_VH
10-0720-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0720-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0720-m_VL	IMGT	Sequence Fragment	DIVLTQSPASLAVSLGQRATISCRAS	ESVDTYG YMF	LHWYQQKPGQP PKLLIY	RAS	NLESGIPARFSGSGSRTDFTLTINPVEAD DVATYYCQQSNEDPFTFGGGTKLEIK	CQQSNEDPFT	FGGGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASESV DTYGMFLHWYQQKPGQPPKLLIYRAS NLESGIPARFSGSGSRTDFTLTINPVEAD DVATYYCQQSNEDPFTFGGGTKLEIK	10-0720-m_VL
10-0720-m_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57-92	93 - 101	102 - 111		10-0720-m_VL
10-0720-m_VL	IMGT	Length	26	10	17	3	36	9	10		10-0720-m_VL

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0724-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0724-m_VH	IMGT	Sequence Fragment	DVQLQESGPGLVKPSQSLSLTCTVTGY SISDYAWNWIRQFPGNKLEWMGYIT	GYSITSDY A	WNWIRQFPGNK LEWMGY	ITYSGTT	RYNPSLKSRISITRDTSKN HFFLQLSSVTTEDTATYYC	ARGFWYFDV	WGAGTTVTVSS	DVQLQESGPGLVKPSQSLSLTCTVTGYS ITSDYAWNWIRQFPGNKLEWMGYITY SGTTRYNPSLKSRISITRDTSKNHFFLQLS SLTTEDTATYYCARGFWYFDVWGAGT AVTVSS	10-0724-m_VH
10-0724-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0724-m_VH
10-0724-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0724-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0724-m_VL	IMGT	Sequence Fragment	DIVLTQSPASLAVSLGQRATISCRAS	ESVDTYG YMF	LHWYQQKPGQP PKLLIY	RAS	NLESGIPARFSGSGSRTDFTLTINPVEAD DVATYYCQQSNEDPFTFGGGTKLEIK	CQQSNEDPFT	FGGGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASESV DTYGMFLHWYQQKPGQPPKLLIYRAS NLESGIPARFSGSGSRTDFTLTINPVEA DDVATYYCQQSNEDPFTFGGGTKLEIK	10-0724-m_VL
10-0724-m_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57-92	93 - 101	102 - 111		10-0724-m_VL
10-0724-m_VL	IMGT	Length	26	10	17	3	36	9	10		10-0724-m_VL

Table 17: Mouse V_H, V_L, CDR and FR sequences from chimeric anti-P2RY8 antibodies, 10-0725-m and 10-0728-m

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0725-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0725-m_VH	IMGT	Sequence Fragment	DVQLQESGPGLVKPSQ SLSLTCTVT	GYSITSDY A	WNWIRQFPGNK LEWMGY	ITYSGST	RYNPSLKSRISITRDTSKNHFFLQLS SVTTEDIATYYCARGFWYFDVWGAGT AVTVSS	ARGFWYFDV	WGAGTAVTVSS	DVQLQESGPGLVKPSQSLSLTCTVTGYS ITSDYAWNWIRQFPGNKLEWMGYITY SGTTRYNPSLKSRISITRDTSKNHFFLQLS SLTTEDIATYYCARGFWYFDVWGAGT AVTVSS	10-0725-m_VH
10-0725-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0725-m_VH
10-0725-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0725-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0725-m_VL	IMGT	Sequence Fragment	QAVVTQESALTTSPGETVTLTCRSTGA VTLTGNS	TGAVTTS NY	AWVQEKPDHL FTGLIG	GTN	WGAPGVPARFSGSLIGDKAALTITGAQTE DEAIYFCALWYSNHWVFGGGTKLTVL	ALWYSNHWV	FGGGTKLTVL	QAVVTQESALTTSPGETVTLTCRSTGA VTTSNYANWVQEKPDHLFTGLIGGTNN KAPGVPARFSGSLIGDKAALTITGAQTE DEAIYFCALWYSNHWVFGGGTKLTVL	10-0725-m_VL
10-0725-m_VL	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 54	55-90	91 - 99	100 - 109		10-0725-m_VL
10-0725-m_VL	IMGT	Length	25	9	17	3	36	9	10		10-0725-m_VL

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0728-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0728-m_VH	IMGT	Sequence Fragment	EVKLEESGGGLVQPGG SMKLSCAAS	GFTFSDA W	MDWVRQSPEKG LEWVAE	IRSKANN HAT	YYAESVKGRFTISRDDSKS SVYLQMNSLRAEDTGIYY C	TGFAMTTAWFA Y	WGQGTLVTVSS	EVKLEESGGGLVQPGGSMKLSCAASGF TFSDAWMDWVRQSPEKGLEWVAEIRS KANNHATYAESVKGRFTISRDDSKSSV YLQMNSLRAEDTGIYYCTGFAMTTAWF AYWGQGTLVTVSS	10-0728-m_VH
10-0728-m_VH	IMGT	Residues	1 - 25	26 - 33	34 - 50	51 - 60	61 - 98	99 - 110	111 - 121		10-0728-m_VH
10-0728-m_VH	IMGT	Length	25	8	17	10	38	12	11		10-0728-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0728-m_VL	IMGT	Sequence Fragment	ENVLTQSPAIMSASLGE KVTMSCRAS	SSVNY	MYWYQQKSDAS PKLWIY	YTS	NLASGVPAHFRGSGSGNS YSLTISSMEGEDAATYYC	QQFTSSPYT	FGGGTRLEIK	ENVLTQSPAIMSASLGEKVTMSCRASSS VNYMYWYQQKSDASPKLWIYYTSNLA PGVPAHFRGSGSGNSYSLTISSMEGEDA ATYYCQQFTSSPYTFGGGTKLEIK	10-0728-m_VL
10-0728-m_VL	IMGT	Residues	1 - 26	27 - 31	32 - 48	49 - 53	52 - 87	88 - 96	97 - 106		10-0728-m_VL
10-0728-m_VL	IMGT	Length	26	5	17	3	36	9	10		10-0728-m_VL

Table 18: Mouse V_H, V_L, CDR and FR sequences from chimeric anti-P2RY8 antibody, 10-0729-m

Mouse VH and VL sequences from chimeric anti-P2RY8 antibody of 10-0729-m

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0729-m_VH	IMGT	Sequence Fragment	DVQLQESGPGLVKPSQSLSLTCTVT SLXLTCTVT	GYSITSDF A	WNWIRQVPGNK LEWMGY	ISYSGTT	RYNPSLKSRITITQDTSKN QFFLQLNSVTPEDTATYY C	ARGWNYDV	WGAGTTVTVSS	DVQLQESGPGLVKPSQSLSLTCTVTGYS ITSDFAWNWIRQVPGNKLEWMGYISY SGTTRYNPSLKSRITITQDTSKNQFFLQL NSVTPEDTATYYCARGWNYDVWGAG TTVTVSS	10-0729-m_VH
10-0729-m_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0729-m_VH
10-0729-m_VH	IMGT	Length	25	9	17	7	38	9	11		10-0729-m_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0729-m_VL	IMGT	Sequence Fragment	DIVLTQSPASLAVSLGQRATISCRAS	QSVDSYGN TF	MHWYQHKPGQ SPRLLIY	RAS	NLESGIPARFSGSGSRTDFTLTINPVEADDVATYYC	QQSNEDPYT	FGGGTQLEVK	DIVLTQSPASLAVSLGQRATISCRASESV DSYGTTFMHWYQHKPGQSPRLLIYRAS NLESGIPARFSGSGSRTDFTLTINPVEAD DVATYYCQQSNEDPYTFGGGTQLEVK	10-0729-m_VL
10-0729-m_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0729-m_VL
10-0729-m_VL	IMGT	Length	26	10	17	3	36	9	10		10-0729-m_VL

Table 19: Humanized V_H, V_L, CDR and FR sequences from humanized anti-P2RY8 antibodies, 10-0716-h1 and 10-0716-h2

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h1

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h1_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGGSLRLSCAVSGY	GYSITSDY	WNWIRQAPGKG LEWVSY	ITYSGTT	TYNPSLKSRFTISRDTSKN TFYLQMNSLRAEDTAVYY C	ARGYWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWVSYITY SGTTYNPSLKSRFTISRDTSKNTFYLQM 10-0716-h1_VH KSLRAEDTAVYYCARGYWYFDVWGQG TTVTVSS	
10-0716-h1_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h1_VH
10-0716-h1_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h1_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h1_VL	IMGT	Sequence Fragment	DIQMTQSPSSLSASVGD RATITCRAS	ESVDSYGY TF	LFWYQQKPGK APKLLIY	RAS	NVESGVPSRFSGSGSGTD FTLTISSLQPEDFATYYC	CQQSNEDPFT	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASES VDSYGYTFMHWYQQKPGKAPKLLIYRA SNVESGVPSRFSGSGSGTDFTLTISSLQP EDFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h1_VL
10-0716-h1_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h1_VL
10-0716-h1_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h1_VL

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h2

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h2_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGGSLRLSCAVSGY	GYSITSDY	WNWIRQAPGKG LEWVSY	ITYSGTT	TYNPSLKSRFTISRDTSKN TFYLQMNSLRAEDTAVYY C	ARGYWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWVSYITY SGTTYNPSLKSRFTISRDTSKNTFYLQM 10-0716-h2_VH KSLRAEDTAVYYCARGYWYFDVWGQG TTVTVSS	
10-0716-h2_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h2_VH
10-0716-h2_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h2_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h2_VL	IMGT	Sequence Fragment	DIQLTQSPSSLSASVGDRATITCRAS	ESVDSYGY TF	LFWYQQKPGK APKLLIY	RAS	NVESGIPSRFSGSGSGTDF TLTISSVQPEDFATYYC	CQQSNEDPFT	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESV DSYGYTFMHWYQQKPGKAPKLLIYRAS NVESGIPSRFSGSGSGTDFTLTISSVQPE DFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h2_VL
10-0716-h2_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h2_VL
10-0716-h2_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h2_VL

Table 20: Humanized V_H, V_L, CDR and FR sequences from humanized anti-P2RY8 antibodies, 10-0716-h3 and 10-0716-h4

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h3

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h3_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGG SLRLSCAVS	GYSITSDY A	WNWIRQAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGYWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWMGYIT YSGTTYNPSLKSRITISRDTSKNTFYLQL NSVRAEDTAVYYCARGYWYFDVWGQ GTTVTVSS	10-0716-h3_VH
10-0716-h3_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h3_VH
10-0716-h3_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h3_VH

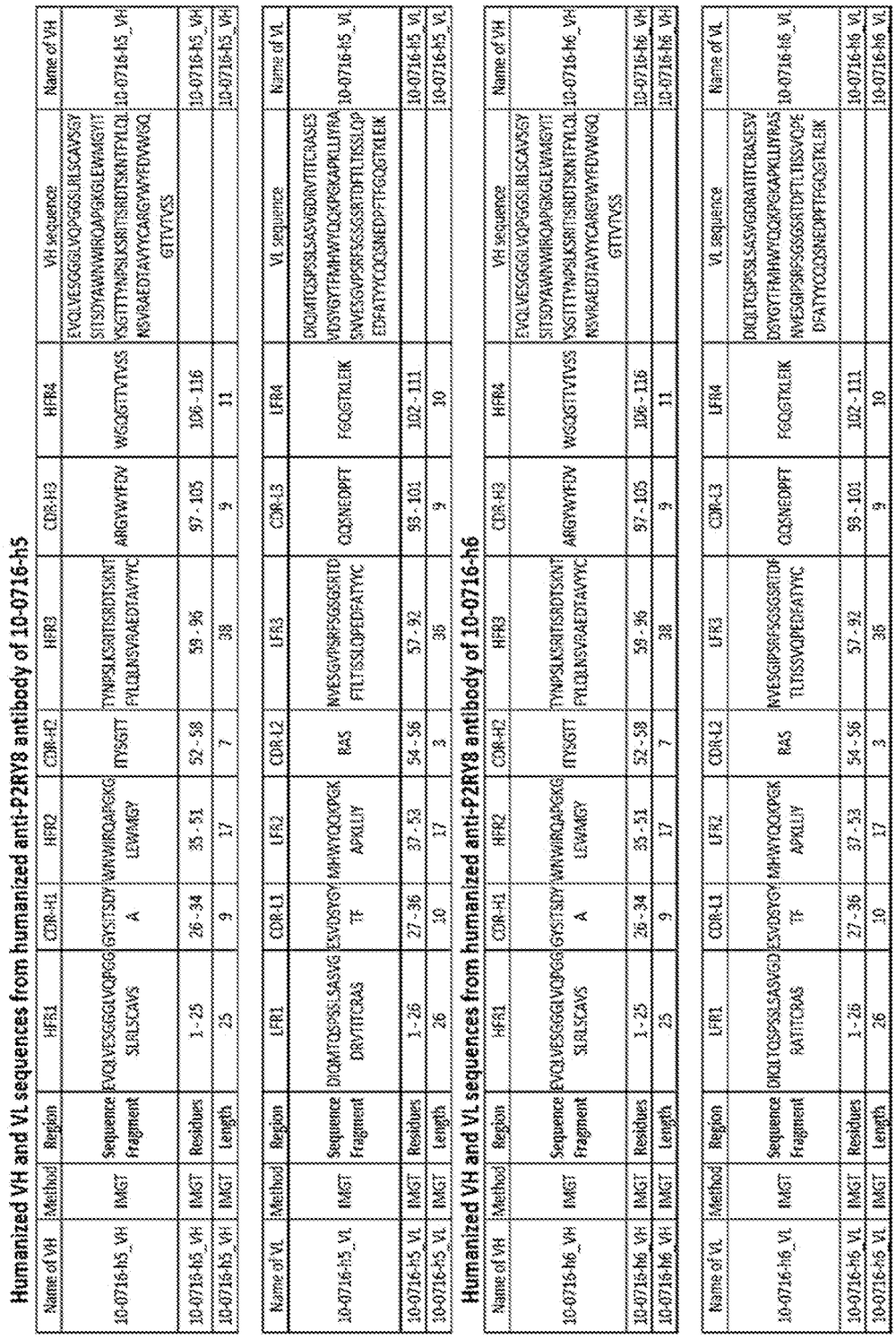
Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h3_VL	IMGT	Sequence Fragment	DIQMTQSPSSLSASVG DRVTITCRAS	QSVDSNGY TF	LNWYQQKPGK APKLLIY	RAS	WESGVPSRFSGSGSGTD FTLTISSLQPEDFATYYC	QQSNEDPFT	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASES VDSYGYTFMNWYQQKPGKAPKLLIYRA SNVESGVPSRFSGSGSGTDFTLTISSLQP EDFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h3_VL
10-0716-h3_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h3_VL
10-0716-h3_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h3_VL

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h4

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h4_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGG SLRLSCAVS	GYSITSDY A	WNWIRQAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGYWYFDV	WGQGTTVTVSS	QLVESGGGLVQPGGSLRLSCAVSGYSIT SDYAWNWIRQAPGKGLEWMGYITYSG TTYNPSLKSRITISRDTSKNTFYLQLNSV RAEDTAVYYCARGYWYFDVWGQGTTV TVSS	10-0716-h4_VH
10-0716-h4_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h4_VH
10-0716-h4_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h4_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h4_VL	IMGT	Sequence Fragment	DIQLTQSPSSLSASVGDR ATITCRAS	QSVDSYGY TF	MHWYQQKPGK APKLLIY	RAS	WESGIPSRFSGSGSGTDF TLTISSVQPEDFATYYC	QQSNEDPFT	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESV DSYGYTFMHWYQQKPGKAPKLLIYRAS NVESGIPSRFSGSGSGTDFTLTISSVQPE DFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h4_VL
10-0716-h4_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h4_VL
10-0716-h4_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h4_VL

Table 21: Humanized V_H, V_L, CDR and FR sequences from humanized anti-P2RY8 antibodies, 10-0716-h5 and 10-0716-h6



Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h5

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h5_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGG SLRLSCAVS	GYSITSDY A	WNWIRQAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGYWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWMGYIT YSGTTYNPSLKSRITISRDTSKNTFYLQLN KSVRAEDTAVYYCARGYWYFDVWGQ GTTVTVSS	10-0716-h5_VH
10-0716-h5_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h5_VH
10-0716-h5_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h5_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h5_VL	IMGT	Sequence Fragment	DIQMTQSPSSLSASVG DRVTITCRAS	ESVDSYGY TF	MHWYQQKPGK APKLLIY	RAS	NVESGVPSRFSGSGSRTD FTLTISSLQPEDFATYYC	QQSNEDPFT	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASES VDSYGYTFMHWYQQKPGKAPKLLIYRA SNVESGVPSRFSGSGSRTDFTLTISSLQP EDFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h5_VL
10-0716-h5_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h5_VL
10-0716-h5_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h5_VL

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h6

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h6_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGG SLRLSCAVS	GYSITSDY A	WNWIRQAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGYWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWMGYIT YSGTTYNPSLKSRITISRDTSKNTFYLQLN KSVRAEDTAVYYCARGYWYFDVWGQ GTTVTVSS	10-0716-h6_VH
10-0716-h6_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h6_VH
10-0716-h6_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h6_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h6_VL	IMGT	Sequence Fragment	DIQLTQSPSSLSASVGD RATITCRAS	ESVDSYGY TF	MHWYQQKPGK APKLLIY	RAS	NVESGIPSRFSGSGSRTDF TLTISSVQPEDFATYYC	QQSNEDPFT	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESV DSYGYTFMHWYQQKPGKAPKLLIYRAS NVESGIPSRFSGSGSRTDFTLTISSVQPE DFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h6_VL
10-0716-h6_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h6_VL
10-0716-h6_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h6_VL

Table 22: Humanized V_H, V_L, CDR and FR sequences from humanized anti-P2RY8 antibodies, 10-0716-h8 and 10-0724-h3

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0716-h8

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0716-h8_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGGSLRLSCAVSGY SLRLSCAVS	GYSTSDY A	WAWIRQAPGKG LEWMGY	ITYSGTT	TYADSLKGRFTISRDTSKNTFYLQM TFYLQMNSVRAEDTAVYYCA C	ARGYWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SFSDYAWNWIRQAPGKGLEWMGYIT YSGTTYADSLKGRFTISRDTSKNTFYLQM NSVRAEDTAVYYCARGYWYFDVWGQ GTTVTVSS	10-0716-h8_VH
10-0716-h8_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0716-h8_VH
10-0716-h8_VH	IMGT	Length	25	9	17	7	38	9	11		10-0716-h8_VH

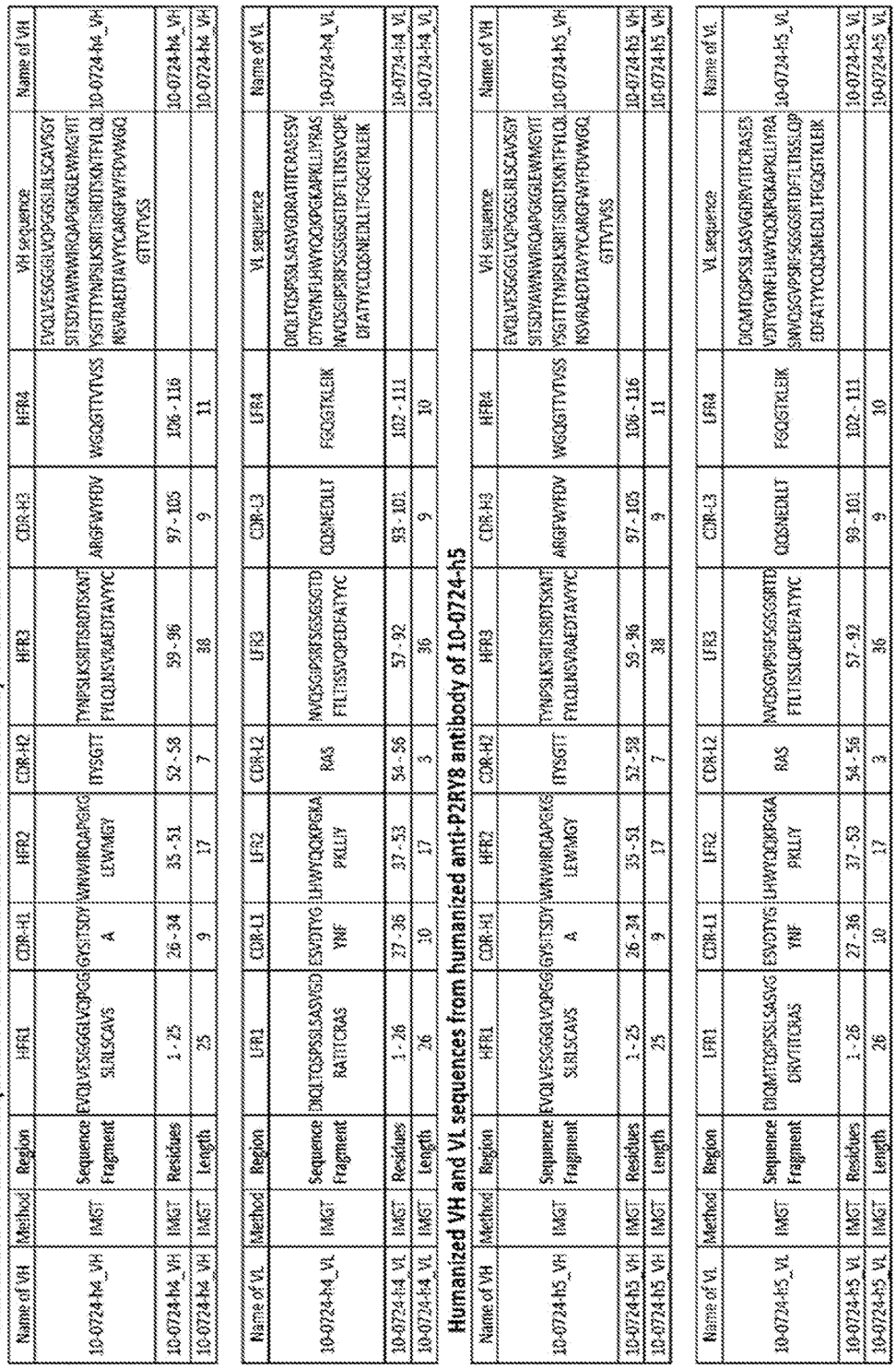
Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0716-h8_VL	IMGT	Sequence Fragment	DIQMTQSPSSLSASVGD DRVTITCRAS	ESVDSYGY TF	MHWYQQKPGK APKLLIY	RAS	NVESGVPSRFSGSGSGTD FTLTISSLQPEDFATYYC	QQSNEDPFT	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASES VDSYGYTFMHWYQQKPGKAPKLLIYRA SNVESGVPSRFSGSGSGTDFTLTISSLQP EDFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h8_VL
10-0716-h8_VL	IMGT	Residues	1 - 26	27 - 38	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0716-h8_VL
10-0716-h8_VL	IMGT	Length	26	10	17	3	36	9	10		10-0716-h8_VL

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0724-h3

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0724-h3_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGGSLRLSCAVSGY SLRLSCAVS	GYSTSDY A	WAWIRQAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGPWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SFSDYAWNWIRQAPGKGLEWMGYIT YSGTTYNPSLKSRITISRDTSKNTFYLQL NSVRAEDTAVYYCARGPWYFDVWGQ GTTVTVSS	10-0724-h3_VH
10-0724-h3_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0724-h3_VH
10-0724-h3_VH	IMGT	Length	25	9	17	7	38	9	11		10-0724-h3_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0724-h3_VL	IMGT	Sequence Fragment	DIQMTQSPSSLSASVGD DRVTITCRAS	ESVDTYG YMF	LHWYQQKPGKA PKLLIY	RAS	NVGSGVPSRFSGSGSGT DFTLTISSLQPEDFATYYC	QQSNEDLIT	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASES VDTYGYMFLHWYQQKPGKAPKLLIYRA SNVGSGVPSRFSGSGSGTDFTLTISSLQ PEDFATYYCQQSNEDLITFGQGTKLEIK	10-0724-h3_VL
10-0724-h3_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0724-h3_VL
10-0724-h3_VL	IMGT	Length	26	10	17	3	36	9	10		10-0724-h3_VL

Table 23: Humanized V_H, V_L, CDR and FR sequences from humanized anti-P2RY8 antibodies, 10-0724-h4 and 10-0724-h5



Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0724-h4

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0724-h4_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGG SLRLSCAVS	GYSTSDY A	WNWIRQAPGKG LEWMGY	ITYSGTT	TYMPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGFWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWMGYIT YSGTTYNPSLKSRITISRDTSKNTFYLQL NSVRAEDTAVYYCARGFWYFDVWGQ GTTVTVSS	10-0724-h4_VH
10-0724-h4_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0724-h4_VH
10-0724-h4_VH	IMGT	Length	25	9	17	7	38	9	11		10-0724-h4_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0724-h4_VL	IMGT	Sequence Fragment	DIQLTQSPSSLSASVGD RATITCRAS	ESVDTYG YNF	LHWYQQKPGKA PKLLIY	RAS	NVQSGVPSRFSGSGSGTD FTLTISSVQPEDFATYYC	QQSNEDLLT	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESV DTYGYNFLHWYQQKPGKAPKLLIYRAS NVQSGVPSRFSGSGSGTDFTLTISSVQPE DFATYYCQQSNEDLLTFGQGTKLEIK	10-0724-h4_VL
10-0724-h4_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0724-h4_VL
10-0724-h4_VL	IMGT	Length	26	10	17	3	36	9	10		10-0724-h4_VL

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0724-h5

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0724-h5_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGG SLRLSCAVS	GYSTSDY A	WNWIRQAPGKG LEWMGY	ITYSGTT	TYMPSLKSRITISRDTSKNT FYLQLNSVRAEDTAVYYC	ARGFWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY SITSDYAWNWIRQAPGKGLEWMGYIT YSGTTYNPSLKSRITISRDTSKNTFYLQL NSVRAEDTAVYYCARGFWYFDVWGQ GTTVTVSS	10-0724-h5_VH
10-0724-h5_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 58	59 - 96	97 - 105	106 - 116		10-0724-h5_VH
10-0724-h5_VH	IMGT	Length	25	9	17	7	38	9	11		10-0724-h5_VH

Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0724-h5_VL	IMGT	Sequence Fragment	DIQMTQSPSSLSASVG DRVTITCRAS	ESVDTYG YNF	LHWYQQKPGKA PKLLIY	RAS	NVQSGVPSRFSGSGSRTD FTLTISSLQPEDFATYYC	QQSNEDLLT	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASES VDTYGYNFLHWYQQKPGKAPKLLIYRA SNVQSGVPSRFSGSGSRTDFTLTISSLQP EDFATYYCQQSNEDLLTFGQGTKLEIK	10-0724-h5_VL
10-0724-h5_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0724-h5_VL
10-0724-h5_VL	IMGT	Length	26	10	17	3	36	9	10		10-0724-h5_VL

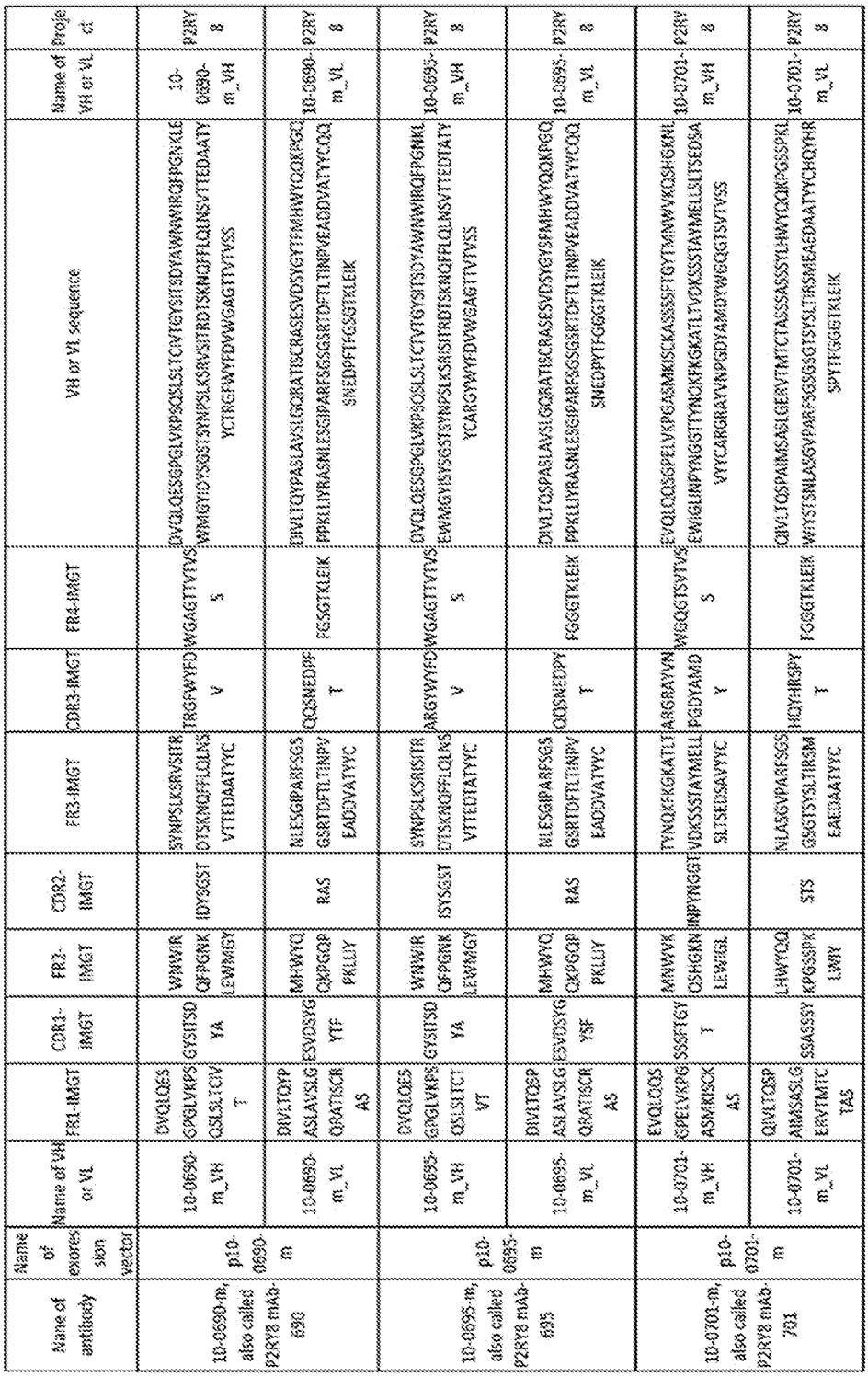
Table 24: Humanized V_H, V_L, CDR and FR sequences from humanized anti-P2RY8 antibody, 10-0724-h6

Humanized VH and VL sequences from humanized anti-P2RY8 antibody of 10-0724-h6

Name of VH	Method	Region	HFR1	CDR-H1	HFR2	CDR-H2	HFR3	CDR-H3	HFR4	VH sequence	Name of VH
10-0724-h6_VH	IMGT	Sequence Fragment	EVQLVESGGGLVQPGGSLRLSCAVS	GYSITSDY	WVRQAPGKG	ITYSGTT	TYNPSLKSRITISKDTSKNTFYLQL PYLDLKSVRAEDTAVYCARGPWYFDVWGQ	ARGPWYFDV	WGQGTTVTVSS	EVQLVESGGGLVQPGGSLRLSCAVSGY STSDYAWNWIRQAPGKGLEWMGYIT YSGITTYNPSLKSRITISKDTSKNTFYLQL NSVRAEDTAVYCARGPWYFDVWGQ GTTVTVSS	10-0724-h6_VH
10-0724-h6_VH	IMGT	Residues	1 - 25	26 - 34	35 - 51	52 - 59	59 - 96	97 - 105	106 - 116		10-0724-h6_VH
10-0724-h6_VH	IMGT	Length	25	9	17	7	38	9	11		10-0724-h6_VH

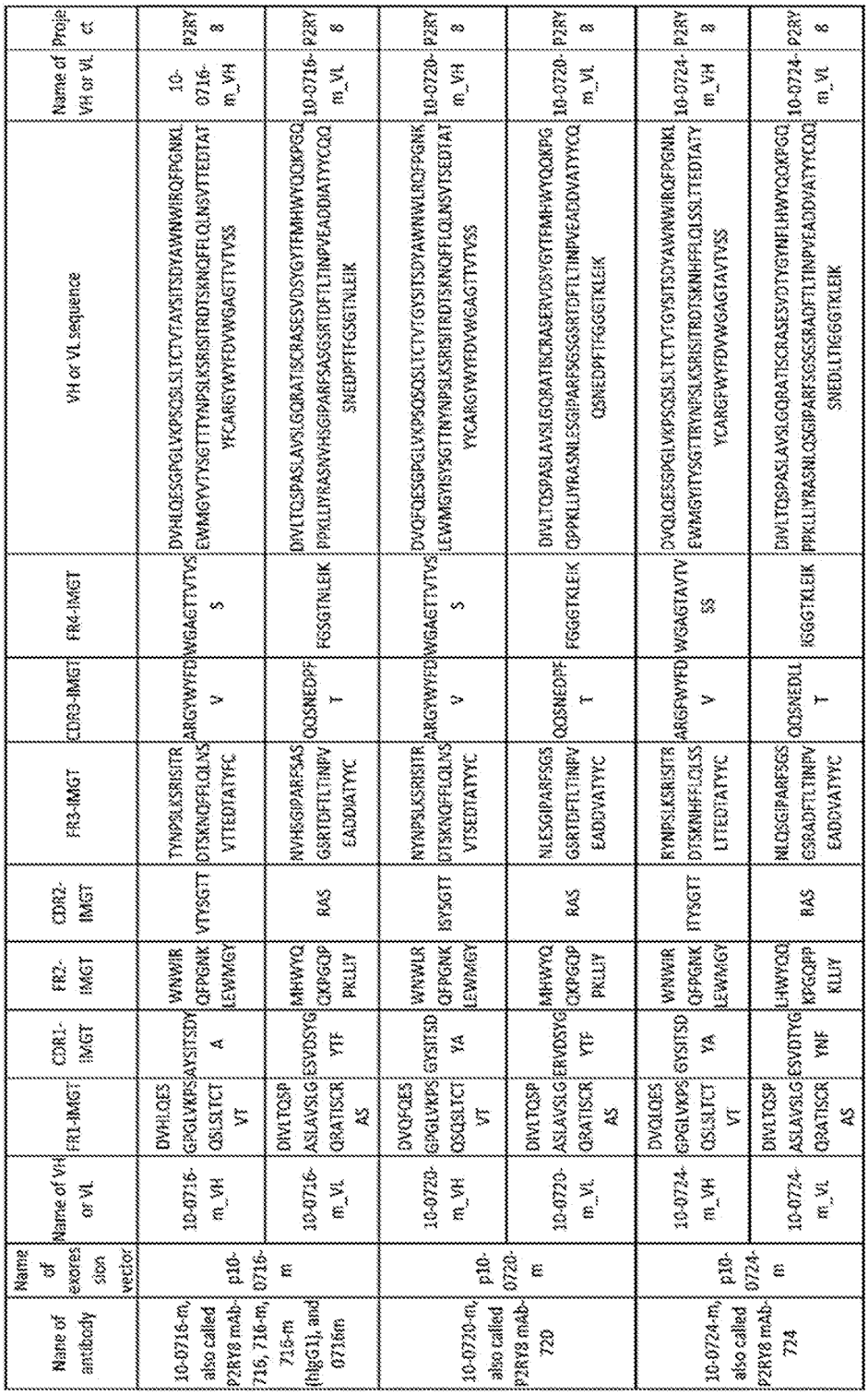
Name of VL	Method	Region	LFR1	CDR-L1	LFR2	CDR-L2	LFR3	CDR-L3	LFR4	VL sequence	Name of VL
10-0724-h6_VL	IMGT	Sequence Fragment	DIQLTQSPSSLSASVGD RATITCRAS	ESVDTYG YMF	LHWYQQKPGKA PKLLIY	RAS	NVQSGIPSRFSGSGSRTD FTLTISSVQPED FATYYC	CQSNEDLLT	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESV DTYGYMFLHWYQQKPGKAPKLLIYRAS NVQSGIPSRFSGSGSRTDFTLTISSVQPE DFATYYCQSNEDLLTFGQGTKLEIK	10-0724-h6_VL
10-0724-h6_VL	IMGT	Residues	1 - 26	27 - 36	37 - 53	54 - 56	57 - 92	93 - 101	102 - 111		10-0724-h6_VL
10-0724-h6_VL	IMGT	Length	26	10	17	3	36	9	10		10-0724-h6_VL

Table 25: Mouse V_H, V_L, CDR and FR sequences of chimeric anti-P2RY8 antibodies, 10-0690-m, 10-0695-m and 10-0701-m, and name of associated expression vector



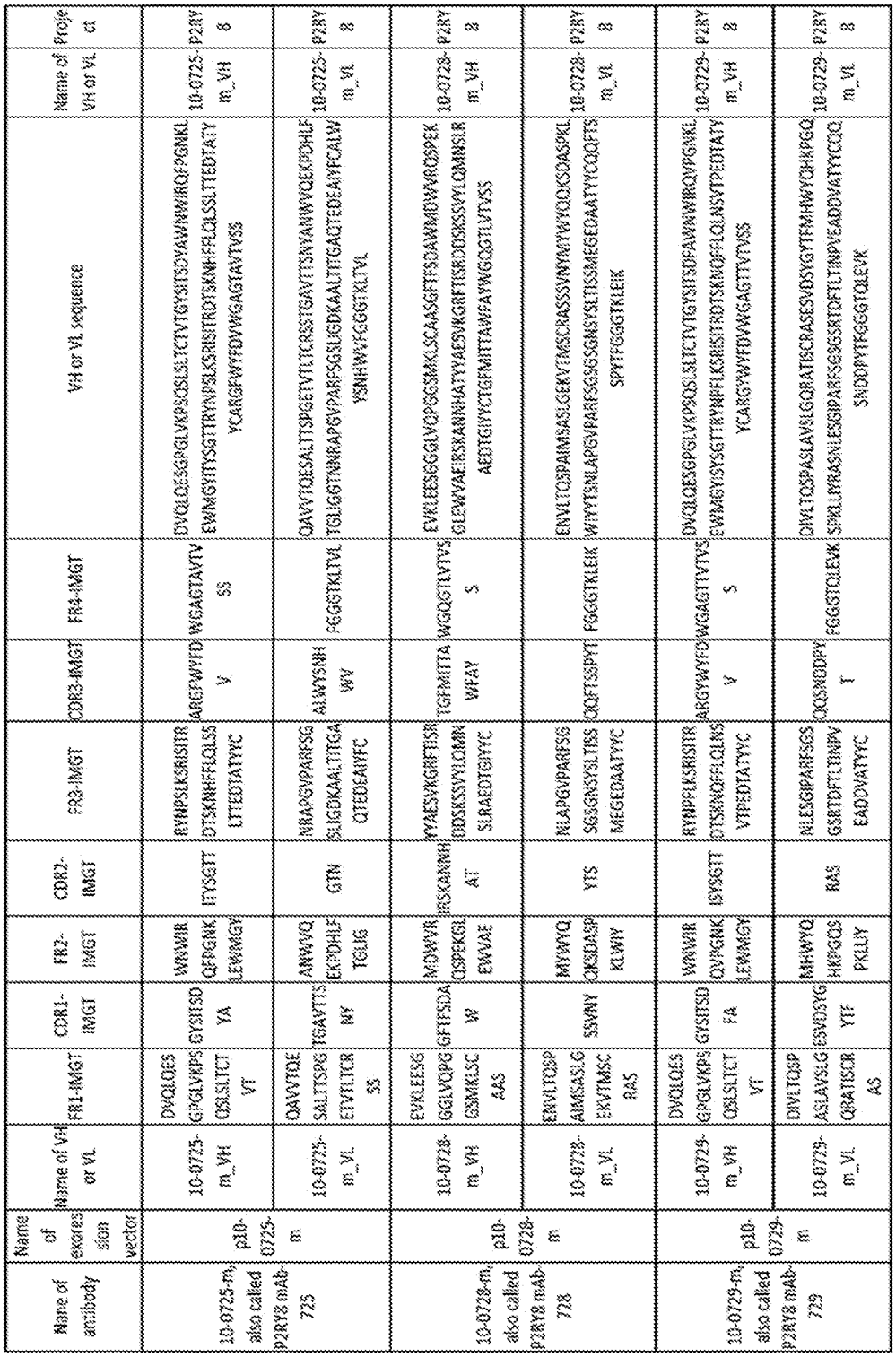
Name of antibody	Name of exoression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Project
10-0690-m, also called P2RY8 mAb-690	p10-0690-m	10-0690-m_VH	DVQLQES GPGLVKPS QSLSLTCV T	GYSITSD YA	WNWIR QFPGNK LEWMGY	IDYSGST	SYNPSLKSRVSITR DTSKNQFFLQLNS VTTEDAATYYC	TRGFWYFDV	WGAGTTVTVS S	DVQLQESGPGLVKPSQSLSLTCNTGYSITSDYAWNWIRQFPGNKLE WMGYIDYSGSTSYNPSLKSRVSITRDTSKNQFFLQLNSVTTEDAATY YCTRGFWYFDVWGAGTTVTVSS	10-0690-m_VH	P2RY8
		10-0690-m_VL	DIVLTQYP ASLAVSLG QRATISCR AS	ESVDSYG YTF	MHWYQ QKPGQP PKLLIY	RAS	NLESGIPARFSGS GSRTDFTLTINPV EADDVATYYC	QQSNEDPF T	FGSGTKLEIK	DIVLTQYPASLAVSLGQRATISCRASESVDSYGYTFMHWYQQKPGQ PPKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQ SNEDPFTFGSGTKLEIK	10-0690-m_VL	P2RY8
10-0695-m, also called P2RY8 mAb-695	p10-0695-m	10-0695-m_VH	QVQLQES GPGLVKPS QSLSLTCT VT	GYSITSD YA	WNWIR QFPGNK LEWMGY	ISYSGST	SYNPSLKSRISITR DTSKNQFFLQLNS VTTEDTATYYC	ARGYWYFDV	WGAGTTVTVS S	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKL EWMGYISYSGSTSYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTATY YCARGYWYFDVWGAGTTVTVSS	10-0695-m_VH	P2RY8
		10-0695-m_VL	DIVLTQSP ASLAVSLG QRATISCR AS	ESVDSYG YSF	MHWYQ QKPGQP PKLLIY	RAS	NLESGIPARFSGS GSRTDFTLTINPV EADDVATYYC	QQSNEDPY T	FGGGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYSFMHWYQQKPGQ PPKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQ SNEDPYTFGGGTKLEIK	10-0695-m_VL	P2RY8
10-0701-m, also called P2RY8 mAb-701	p10-0701-m	10-0701-m_VH	EVQLQQS GPELVKPG ASMRISCK AS	SSSFTGY T	MNWVK QSHGKN LEWIGL	INPYNGGT	TYNQKFKGKATLT VDKSSSTAYMELL SLTSEDSAVYYC	ARSRAYVN PGDYAMD Y	WGQGTSVTVS S	EVQLQQSGPELVKPGASMKISCKASSSFTGYTMNWVKQSHGKNL EWIGLINPYNGGTTYNQKFKGKATLTVDKSSSTAYMELLSLTSEDSA VYYCARSRAYVNPGDYAMDYWGQGTSVTVSS	10-0701-m_VH	P2RY8
		10-0701-m_VL	QIVLTQSP AIMSASLG ERVTMTC TAS	SSASSSY	LHWYQQ KPGSSPK LWIY	STS	NLASGVPAARFSGS GSGTSYSLTISRM EAEDAATYYC	HQYHRSPY T	FGSGTRLEIK	QIVLTQSPAIMSASLGERVTMTCTASSSASSSYLHWYQQKPGSSPKL WIYSTSNLASGVPARFSGSGSGTSYSLTISRMEAEDAATYYCHQYHR SPYTFGSGTRLEIK	10-0701-m_VL	P2RY8

Table 26: Mouse V_H, V_L, CDR and FR sequences of chimeric anti-P2RY8 antibodies, 10-0716-m, 10-0720-m and 10-0724-m, and name of associated expression vector



Name of antibody	Name of expression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Project
10-0716-m, also called P2RY8 mAb-716, 716-m, 716-m (hIgG1), and 0716m	p10-0716-m	10-0716-m_VH	DVHLQES GPGLVKPS QSLSLTCT VT	GYSITSDY A	WNWIR QFPGNK LEWMGY	VTYSGTT	TYNPSLKSRISITR DTSKNQFFLQLNS VTTEDTATYFC	ARGYWYFDVWGAGTTVTVSS	WGAGTTVTVS S	DVHLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKL EWMGYVTYSGTTYNPSLKSRISITRDTSKNQFFLQLNSVTTEDTAT YFCARGYWYFDVWGAGTTVTVSS	10-0716-m_VH	P2RY8
		10-0716-m_VL	DIVLTQSP ASLAVSLG QRATISCR AS	ESVDSYG YTF	MHWYQ QKPGQP PKLLIY	RAS	NVHSGIPARFSAS GSRTDFTLTINPV EADDVATYYC	QQSNEDPF T	FGSGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYTFMHWYQQKPGQ PPKLLIYRASNVHSGIPARFSASGSRTDFTLTINPVEADDVATYYCQQ SNEDPFTFGSGTKLEIK	10-0716-m_VL	P2RY8
10-0720-m, also called P2RY8 mAb-720	p10-0720-m	10-0720-m_VH	QVQFQES GPGLVKPS QSQSLTCT VT	GYSITSD YA	WNWLR QFPGNK LEWMGY	ISYSGTT	NYNPSLKSRISITR DTSKNQFFLQLNS VTSEDTATYYC	ARGYWYFD V	WGAGTTVTVS S	QVQFQESGPGLVKPSQSQSLTCTVTGYSITSDYAWNWLRQFPGNK LEWMGYISYSGTTNYNPSLKSRISITRDTSKNQFFLQLNSVTSEDTAT YYCARGYWYFDVWGAGTTVTVSS	10-0720-m_VH	P2RY8
		10-0720-m_VL	DIVLTQSP ASLAVSLG QRATISCR AS	ESVDSYG YTF	MHWYQ QKPGQP PKLLIY	RAS	NLESGIPARFSGS GSRTDFTLTINPV EADDVATYYC	QQSNEDPF T	FGGGTKLEIK	DIVLTQSPASLAVSLGQRATISCRASERVDSYGYTFMHWYQQKPG QPPKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQ QSNEDPFTFGGGTKLEIK	10-0720-m_VL	P2RY8
10-0724-m, also called P2RY8 mAb-724	p10-0724-m	10-0724-m_VH	DVQLQES GPGLVKPS QSLSLTCT VT	GYSITSD YA	WNWIR QFPGNK LEWMGY	ITYSGTT	RYNPSLKSRISITR DTSKNHFFLQLSS VTTEDTATYYC	ARGFWYFD V	WGAGTTVTV SS	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDYAWNWIRQFPGNKL EWMGYITYSGTTRYNPSLKSRISITRDTSKNHFFLQLSSVTTEDTATY YCARGFWYFDVWGAGTTVTVSS	10-0724-m_VH	P2RY8
		10-0724-m_VL	DIVLTQSP ASLAVSLG QPATISCR AS	ESVDTYG YNF	LHWYQQ KPGQPP KLLIY	RAS	NLDSGIPARFSGS GSRADFTLTINPV EADDVATYYC	QQSNEDLL T	RGGGTKLEIK	DIVLTQSPASLAVSLGQPATISCRASESVDTYGYNFLHWYQQKPGQ PPKLLIYRASNLQSGIPARFSGSGSRADFTLTINPVEADDVATYYCQQ SNEDLLTFGGGTKLEIK	10-0724-m_VL	P2RY8

Table 27: Mouse V_H, V_L, CDR and FR sequences of chimeric anti-P2RY8 antibodies, 10-0725-m, 10-0728-m and 10-0729-m, and name of associated expression vector

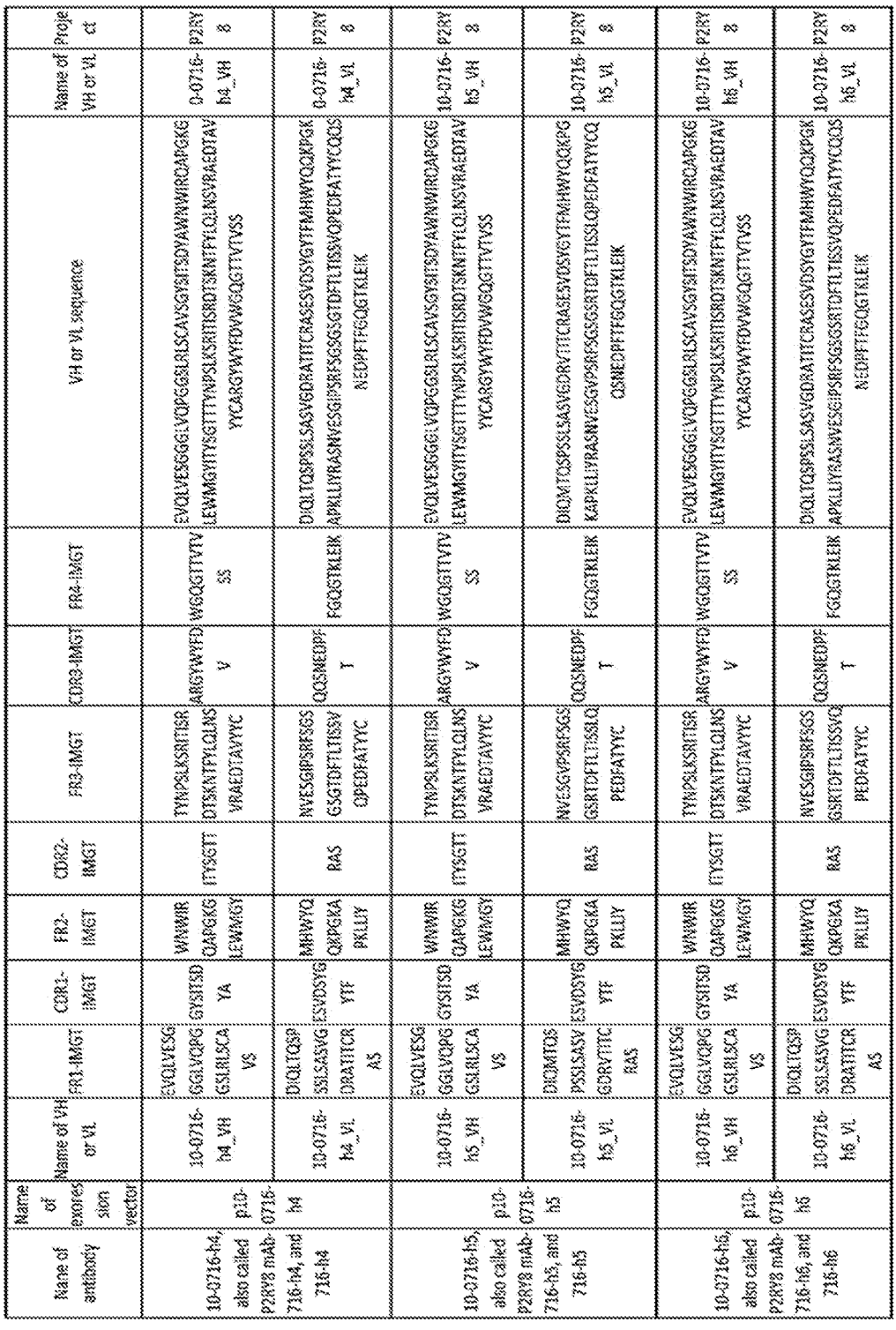


Name of antibody	Name of expression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Project
10-0725-m, also called P2RY8 mAb-725	p10-0725-m	10-0725-m_VH	DVQLQES GPGLVKPS QSLSLTCT VT	GYSITSD FA	WNWIR QFPGNK LEWMGY	ISYSGTT	RYNPSLKSRISITR DTSKNHFFLQLSS LTTEDTATYYC	ARGFWYFD V	WGAGTAVTV SS	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDFAWNWIRQFPGNKL EWMGYITYSGTTRYNPSLKSRISITRDTSKNHFFLQLSSLTTEDTATY YCARGFWYFDVWGAGTAVTVSS	10-0725-m_VH	P2RY8
		10-0725-m_VL	QAVVTQE SALTTSPG ETVTLTCR SS	TGAVTTS NY	ANWVQ EKPDHLF TGLIG	GTN	NRAPGVPARFSG SLIGDKAALTITGA QTEDEAIYFC	ALWYSNH WV	FGGGTKLTVL	QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDHLF TGLIGGTNNRAPGVPARFSGSLIGDKAALTITGAQTEDEAIYFCALW YSNHWVFGGGTKLTVL	10-0725-m_VL	P2RY8
10-0728-m, also called P2RY8 mAb-728	p10-0728-m	10-0728-m_VH	EVKLEESG GGLVQPG GSMKLSC AAS	GFTFSDA W	MDWVR QSPEKGL EWVAE	IRSKANNH AT	TYAESVKGRFTISR DDSKSSVYLQMN SLRAEDTGIYYC	TGFMITTA WFAY	WGQGTLVTVS S	EVKLEESGGGLVQPGGSMKLSCAASGFTFSDAWMDWVRQSPEK GLEWVAEIRSKANNHATYYAESVKGRFTISRDDSKSSVYLQMNSLR AEDTGIYYCTGFMITTAWFAYWGQGTLVTVSS	10-0728-m_VH	P2RY8
		10-0728-m_VL	ENWLTQS PAIMSAS LGEKVTM SCRASSS WYQQKSD ASPKL	YTS	MYWYQ QKSDASP KLWIY	YTS	NLAPGVPARFSG SGSGNSYSLTISS MEGEDAATYYC	CQQFTSPYT	FGGGTKLEIK	ENWLTQSPAIMSASLGEKVTMSCRASSSWYQQKSDASPKL WIYYTSNLAPGVPARFSGSGSGNSYSLTISSMEGEDAATYYCQQFTS SPYTFGGGTKLEIK	10-0728-m_VL	P2RY8
10-0729-m, also called P2RY8 mAb-729	p10-0729-m	10-0729-m_VH	DVQLQES GPGLVKPS QSLSLTCT VT	GYSITSD FA	WNWIR QYPGNK LEWMGY	ISYSGTT	RYNPFLKSRISITR DTSINQFFLQLNS VTPEDTATYYC	ARGYWYFD W	WGAGTTVTVS S	DVQLQESGPGLVKPSQSLSLTCTVTGYSITSDFAWNWIRQYPGNKL EWMGYISYSGTTRYNPFLKSRISITRDTSINQFFLQLNSVTPEDTATY YCARGYWYFDVWGAGTTVTVSS	10-0729-m_VH	P2RY8
		10-0729-m_VL	DIVLTQSP ASLAVSL GQRATISCR AS	ESVDSYG YTF	MHWYQ HKPGQS PKLLIY	RAS	NLESGIPARFSGS GSRTDFTLTINPV EADDVATYYC	QQSNEDPY T	FGGGTQLEVK	DIVLTQSPASLAVSLGQRATISCRASESVDSYGYTFMHWYQHKPGQ SPKLLIYRASNLESGIPARFSGSGSRTDFTLTINPVEADDVATYYCQQ SNEDPYTFGGGTQLEVK	10-0729-m_VL	P2RY8

Table 28: V_H, V_L, CDR and FR sequences of humanized anti-P2RY8 antibodies, 10-0716-h1, 10-0716-h2 and 10-0716-h3, and name of associated expression vector

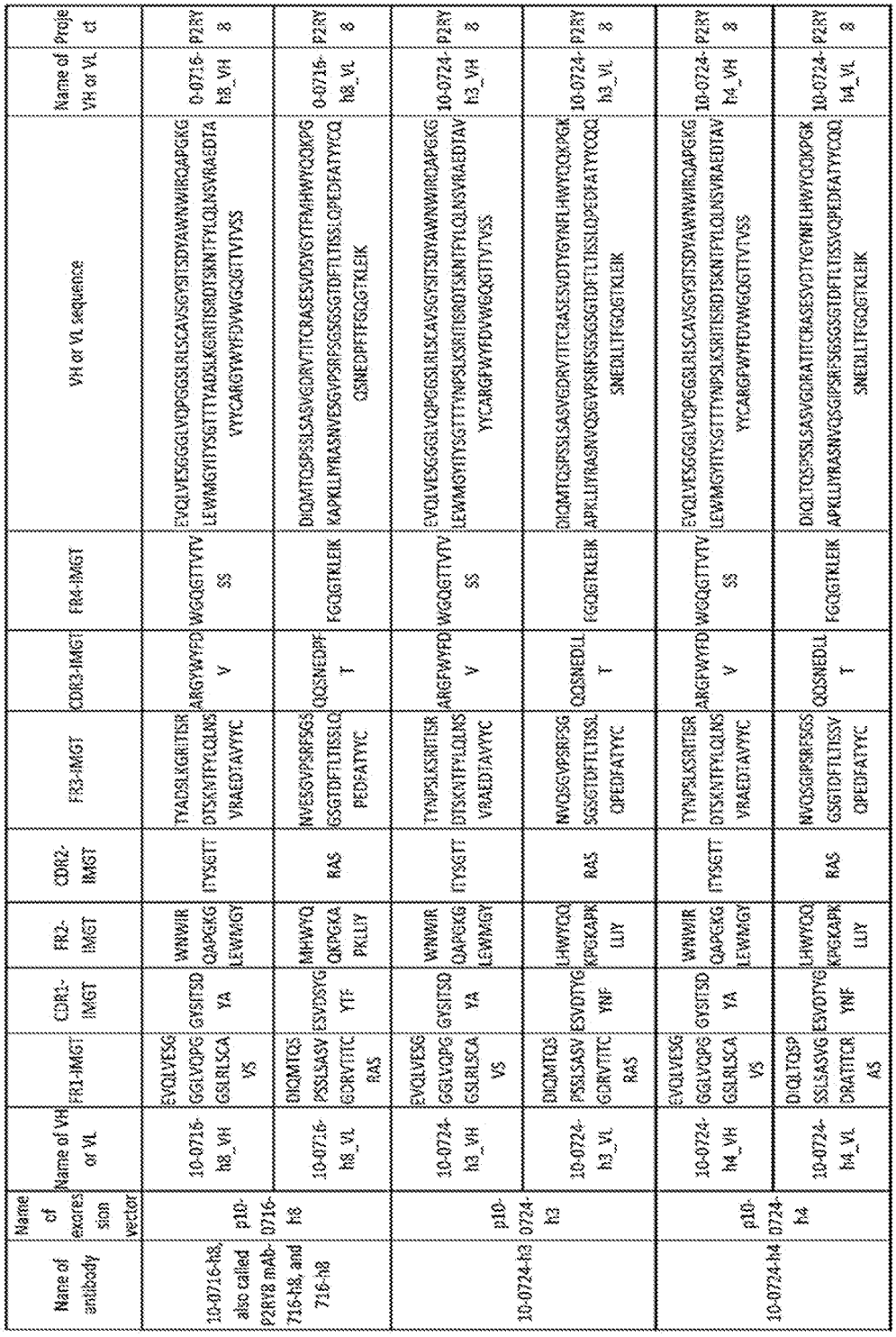
Name of antibody	Name of expression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Project
10-0716-h1, also called P2RY8 mAb-716-h1, and 716-h1	p10-0716-h1	10-0716-h1_VH	EVQLVESGG GLVQPGGSL RLSCA GSLRLSCA VS	GYSITSD YA	WVWIR QAPGKG LEWVSY	ITYSGTT	TYNPSLKSR FTISRDTSK NTFYLQMN SLRAEDTAVYYC	ARGYWYF DV	WGQGTTV TVSS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAV YYCARGYWYFDVWGQGTTVTVSS	0-0716-h1_VH	P2RY8
		10-0716-h1_VL	DIQMTQS PSSLSASV GDRVTITC RAS	ESVDSYG YTF	MHWYQ QKPGKA PKLLIY	RAS	NVESGVPSRFSGS GSGTDFTLTISSLQ PEDFATYYC	QQSNEDPF T	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGK KAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QSNEDPFTFGQGTKLEIK	0-0716-h1_VL	P2RY8
10-0716-h2, also called P2RY8 mAb-716-h2, and 716-h2	p10-0716-h2	10-0716-h2_VH	EVQLVESGG GLVQPGGSL RLSCA GSLRLSCA VS	GYSITSD YA	WVWIR QAPGKG LEWVSY	ITYSGTT	TYNPSLKSR FTISRDTSK NTAYLQMN SLRAEDTAVYYC	ARGYWYF DV	WGQGTTV TVSS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWVSYITYSGTTTYNPSLKSRFTISRDTSKNTAYLQMNSLRAEDTAV YYCARGYWYFDVWGQGTTVTVSS	10-0716-h2_VH	P2RY8
		10-0716-h2_VL	DIQLTQSP SSLSASVG DRATITCR AS	ESVDSYG YTF	MHWYQ QKPGKA PKLLIY	RAS	NVESGIPSRFSGS GSGTDFTLTISSV QPEDFATYYC	QQSNEDPF T	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGK APKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQS NEDPFTFGQGTKLEIK	10-0716-h2_VL	P2RY8
10-0716-h3, also called P2RY8 mAb-716-h3, and 716-h3	p10-0716-h3	10-0716-h3_VH	EVQLVESGG GLVQPGGSL RLSCA GSLRLSCA VS	GYSITSD YA	WVWIR QAPGKG LEWMGY	ITYSGTT	TYNPSLKSR ITISRDTSK NTFYLQLN SVRAEDTAVYYC	ARGYWYF DV	WGQGTTV TVSS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAV YYCARGYWYFDVWGQGTTVTVSS	10-0716-h3_VH	P2RY8
		10-0716-h3_VL	DIQMTQS PSSLSASV GDRVTITC RAS	ESVDSYG YTF	MHWYQ QKPGKA PKLLIY	RAS	NVESGVPSRFSGS GSGTDFTLTISSLQ PEDFATYYC	QQSNEDPF T	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGK KAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QSNEDPFTFGQGTKLEIK	10-0716-h3_VL	P2RY8

Table 29: V_H, V_L, CDR and FR sequences of humanized anti-P2RY8 antibodies, 10-0716-h4, 10-0716-h5 and 10-0716-h6, and name of associated expression vector



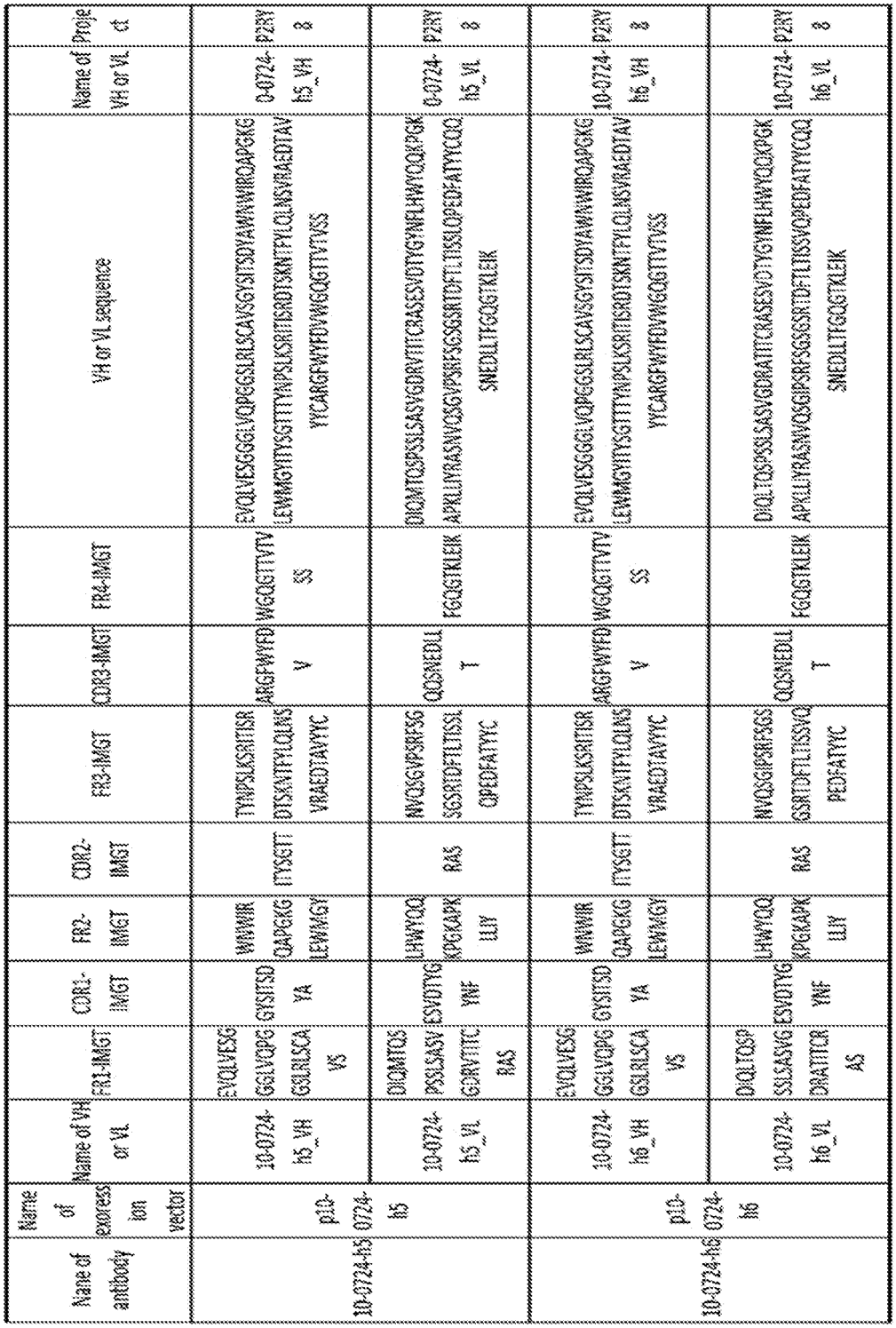
Name of antibody	Name of expression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Project
10-0716-h4, also called P2RY8 mAb-716-h4, and 716-h4	p10-0716-h4	10-0716-h4_VH	EVQLVESGG GLVQPGG SLRLSCA VS	GYSITSD YA	WVRQAPG KGLEWMG	ITYSGTT	TYNPSLK SRITISR DTSKNTF YLQLNSV RAEDTAV YYC	ARGYWYF DV	WGQGTTV TVSS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYITYSGTTYYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDVWGQGTTVTVSS	0-0716-h4_VH	P2RY8
		10-0716-h4_VL	DIQLTQSP SSLSASVG DRATITCR AS	ESVDSYG YTF	MHWYQ QKPGKA PKLLIY	RAS	NVESGIP SRFSGS GSGTDFT LTISSV QPEDFAT YYC	QQSNEDP FT	FGQGTKL EIK	DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEIK	0-0716-h4_VL	P2RY8
10-0716-h5, also called P2RY8 mAb-716-h5, and 716-h5	p10-0716-h5	10-0716-h5_VH	EVQLVESGG GLVQPGG SLRLSCA VS	GYSITSD YA	WVRQAPG KGLEWMG	ITYSGTT	TYNPSLK SRITISR DTSKNTF YLQLNSV RAEDTAV YYC	ARGYWYF DV	WGQGTTV TVSS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYITYSGTTYYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDVWGQGTTVTVSS	10-0716-h5_VH	P2RY8
		10-0716-h5_VL	DIQMTQS PSSLSAS VGDRVTI TC RAS	ESVDSYG YTF	MHWYQ QKPGKA PKLLIY	RAS	NVESGVP SRFSGS GSGSRTD FTLTISS LQPEDFA TYYC	QQSNEDP FT	FGQGTKL EIK	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYRASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h5_VL	P2RY8
10-0716-h5, also called P2RY8 mAb-716-h6, and 716-h6	p10-0716-h6	10-0716-h6_VH	EVQLVESGG GLVQPGG SLRLSCA VS	GYSITSD YA	WVRQAPG KGLEWMG	ITYSGTT	TYNPSLK SRITISR DTSKNTF YLQLNSV RAEDTAV YYC	ARGYWYF DV	WGQGTTV TVSS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEWMGYITYSGTTYYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCARGYWYFDVWGQGTTVTVSS	10-0716-h6_VH	P2RY8
		10-0716-h6_VL	DIQLTQSP SSLSASVG DRATITCR AS	ESVDSYG YTF	MHWYQ QKPGKA PKLLIY	RAS	NVESGIP SRFSGS GSKTDFT LTISSVQ PEDFATY YC	QQSNEDP FT	FGQGTKL EIK	DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPKLLIYRASNVESGIPSRFSGSGSKTDFTLTISSVQPEDFATYYCQQSNEDPFTFGQGTKLEIK	10-0716-h6_VL	P2RY8

Table 30: V_H, V_L, CDR and FR sequences of humanized anti-P2RY8 antibodies, 10-0716-h8, 10-0724-h3 and 10-0724-h4, and name of associated expression vector



Name of antibody	Name of excression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Protein
10-0716-h8, also called P2RY8 mAb-716-h8, and 716-h8	p10-0716-h8	10-0716-h8_VH	EVQLVESG GGLVQPG GSLRLSCA VS	GYSITSD YA	WNWIR QAPGKG LEWMGY	ITYSGTT	TVADSLKGRFTISR DTSKNTFYLQLNS VRAEDTAVYYC	ARGYWYFD V	WGQGTTVTV SS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWMGYITYSGTTYYADSLKGRFTISRDTSKNTFYLQLNSVRAEDTA VYYCARGYWYFDVWGQGTTVTVSS	10-0716-h8_VH	P2RY8
		10-0716-h8_VL	DIQMTQS PSSLSASV GDRVTITC RAS	ESVDSYG YTF	MHWYQ QKPGKA PKLLY	RAS	NVESGVPSRFSGS GSGTDFTLTISSLQ PEDFATYYC	QQSNEDPF T	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPG KAPKLLYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQ QSNEDPFTFGQGTKLEIK	10-0716-h8_VL	P2RY8
10-0724-h3	p10-0724-h3	10-0724-h3_VH	EVQLVESG GGLVQPG GSLRLSCA VS	GYSITSD YA	WNWIR QAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISR DTSKNTFYLQLNS VRAEDTAVYYC	ARGFWYFD V	WGQGTTVTV SS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWMGYITYSGTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAV YYCARGFWYFDVWGQGTTVTVSS	10-0724-h3_VH	P2RY8
		10-0724-h3_VL	DIQMTQS PSSLSASV GDRVTITC RAS	ESVDTYG YMF	LHWYQQ KPGKAPK LLIY	RAS	NVQSGVPSRFSGS SGSGTDFTLTISSL QPEDFATYYC	QQSNEDLL T	FGQGTKLEIK	DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYMFLHWYQQKPGK APKLLIYRASNVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQ SNEDLLTFGQGTKLEIK	10-0724-h3_VL	P2RY8
10-0724-h4	p10-0724-h4	10-0724-h4_VH	EVQLVESG GGLVQPG GSLRLSCA VS	GYSITSD YA	WNWIR QAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISR DTSKNTFYLQLNS VRAEDTAVYYC	ARGFWYFD V	WGQGTTVTV SS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWMGYITYSGTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAV YYCARGFWYFDVWGQGTTVTVSS	10-0724-h4_VH	P2RY8
		10-0724-h4_VL	DIQLTQS SSLSASVG DRATITCR AS	ESVDTYG YMF	LHWYQQ KPGKAPK LLIY	RAS	NVQSGIPSRFSGS GSGTDFTLTISSV QPEDFATYYC	QQSNEDLL T	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESVDTYGYMFLHWYQQKPGK APKLLIYRASNVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQ SNEDLLTFGQGTKLEIK	10-0724-h4_VL	P2RY8

Table 31: V_H, V_L, CDR and FR sequences of humanized anti-P2RY8 antibodies, 10-0724-h5 and 10-0724-h6, and name of associated expression vector



Name of antibody	Name of expression vector	Name of VH or VL	FR1-IMGT	CDR1-IMGT	FR2-IMGT	CDR2-IMGT	FR3-IMGT	CDR3-IMGT	FR4-IMGT	VH or VL sequence	Name of VH or VL	Name of Project
10-0724-h5	p10-0724-h5	10-0724-h5_VH	EVQLVESG GGLVQPG GSLRLSCA VS	GYSITSD YA	WNWIR QAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISR DTSKNTFYLQLNS VRAEDTAVYYC	ARGFWYFDV	WGQGTTVTV SS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWMGYITYSGTTYYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAV YYCARGFWYFDVWGQGTTVTVSS	0-0724-h5_VH	P2RY8
		10-0724-h5_VL	DIQMTQS PSSLSASV GDRVTITC RAS	ESVDTYG YNF	LHWYQQ KPGKAPK LLIY	RAS	NVQSGVPSRFSG SGSRTDFTLTISSL QPEDFATYYC	QQSNEDLL T	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGK APKLLIYRASNVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQ SNEDLLTFGQGTKLEIK	0-0724-h5_VL	P2RY8
10-0724-h6	p10-0724-h6	10-0724-h6_VH	EVQLVESG GGLVQPG GSLRLSCA VS	GYSITSD YA	WNWIR QAPGKG LEWMGY	ITYSGTT	TYNPSLKSRITISR DTSKNTFYLQLNS VRAEDTAVYYC	ARGFWYFDV	WGQGTTVTV SS	EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKG LEWMGYITYSGTTYYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAV YYCARGFWYFDVWGQGTTVTVSS	10-0724-h6_VH	P2RY8
		10-0724-h6_VL	DIQLTQSP SSLSASVG DRATITCR AS	ESVDTYG YNF	LHWYQQ KPGKAPK LLIY	RAS	NVQSGIPSRFSGS GSRTDFTLTISSVQ PEDFATYYC	QQSNEDLL T	FGQGTKLEIK	DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPGK APKLLIYRASNVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQ SNEDLLTFGQGTKLEIK	10-0724-h6_VL	P2RY8

Table 32: Exemplary amino acid sequence of human immunoglobulin light chain constant regions, kappa (IGKC) and lambda 2 (IGLC2), and human immunoglobulin heavy chain constant region, gamma 1 (IGHG1), of humanized P2RY8 antibodies

Name	Description	Sequence
Human Immunoglobulin kappa constant (IGKC)	Uniprot ID: P01834	RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
Human Immunoglobulin lambda constant 2 (IGLC2)	Uniprot ID: P0DOY2	GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADSSPVKAGVETTTPSKQSNNKYA ASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
Human Immunoglobulin heavy constant gamma 1 (IGHG1)	Uniprot ID: P01857	ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSV VTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLM ISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK

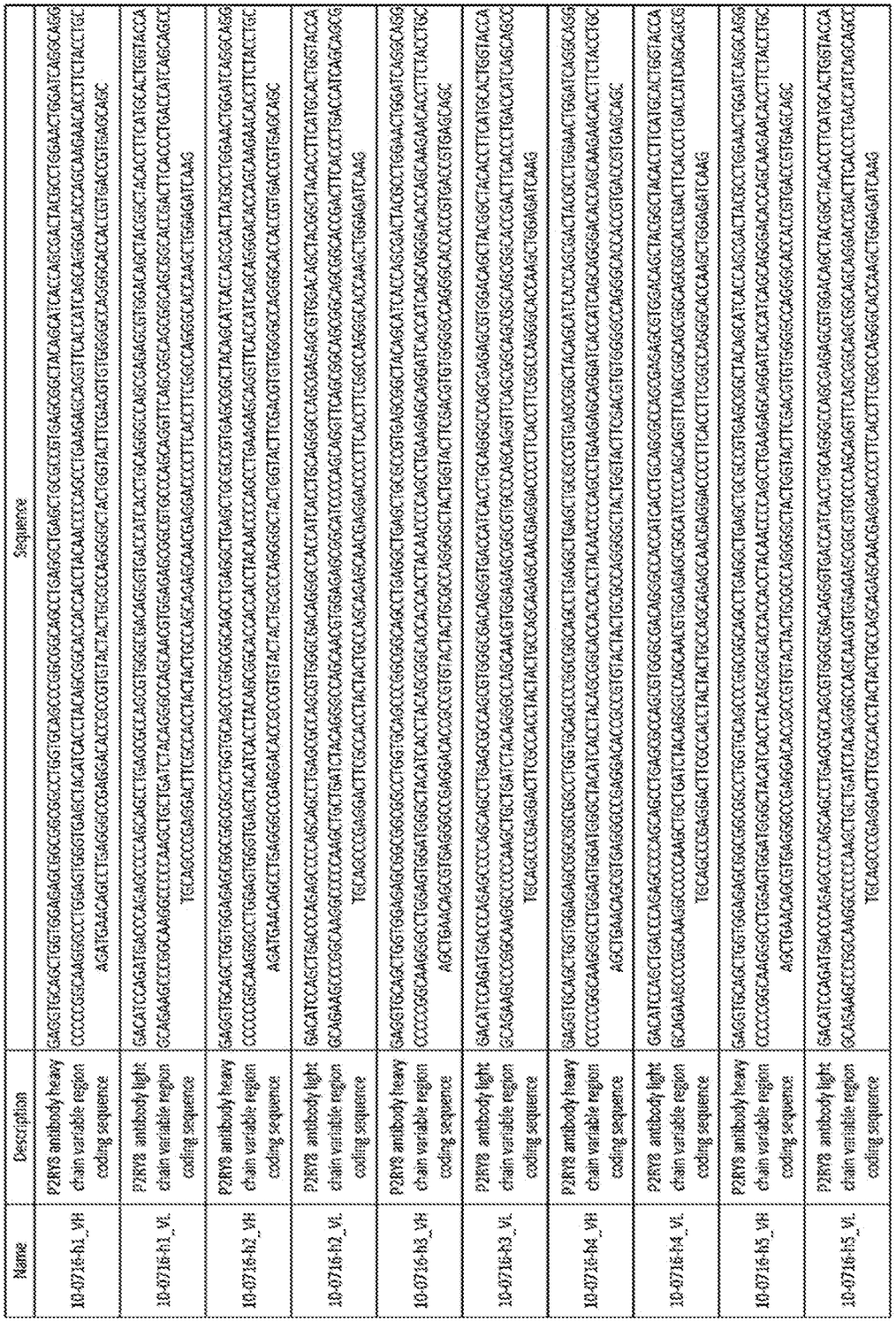
Table 33: Exemplary nucleic acid sequences encoding mouse VH and mouse VL of chimeric P2RY8 antibodies

Name	Description	Sequence
10-0690-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GATGTGCAGCTGCAGGAGAGCGGACCTGGCATGGTGAAGCCTAGCCAGAGCCTGAGCCTCACATGTATCGTGACCGGCTATAGCATCACCTCTGATTACGCCTGGAATTGGATCAGACAGTTTC CAGGGCAACAAGCTGGAATGGATGGGCTACATCGACTACAGCGGCAGCACCTCCTACAACCCCAGCCTGAAAAGCAGAATCGTGATCACACGGGACACCAGCAAGAACCAGTTCTTCCTGCAACT GAACAGCGTGACAACCGTGGCGGCACAGCCGCCTACATACTACTGCGCCAGAGGCTCTCGGTACTTCGACGTGTGGGGCGCCGGCACCACCGTCACAGTGTCTCT
10-0690-m_VL	P2RY8 antibody light chain variable region coding sequence	GATATCGTGCTGACACAGTACCCGGCCTCTCTGGCCGTGTCTCCTGGGCAGCGTGCCTCCATCAGCTGTAGAAGCCTCCGAAAGCGTGGACAGCTACGGCTACACCTTTATGCACTGGTATCAGC AGAAACCTGGACAACCTCCAAAGCTGCTGATCTACCGGGCTTCTAATCTGGAGAGCGGCATCCCTGCTAGATTCAGCGGATCTGGCAGCGAGACCGACTTCACCCTGACAATTAACCCCGTGGA AGCCGACGACGTGGCCACATACTACTGCCAGCAGAGCAACGAGGATCCTTTCACCTTCGGCAGCGGCACCAAGCTGGAGATCAAG
10-0695-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GATGTGCAGCTGCAGGAGTCCGGACCTGGCATGGAAGCCTCTCAGAGCCTGAGCCTCACCTGTACAGTCACCGGCTACAGCATCACCTCTGATTACGCCTGGAATTGGATCAGACACAGTTTC CAGGGCAACAAGCTGGAATGGATGGGCTACATCTCTTATAGCGGCAGCACCTCCTACAACCCCAGCCTGAAAAGCAGAATCAGCATCACACGGGACACCAGCAAGAACCAGTTCTTCCTGCAACT GAACAGCGTGACAACCGAGGACACAGCCACCTACTACTGCGCCAGAGGCTACTGGTACTTCGACGTGTGGGGCGCTACGGCAGCCTGGTCACCGTGTCTGCAGC
10-0695-m_VL	P2RY8 antibody light chain variable region coding sequence	GATATCGTGCTGACACAGAGCCCTGCTCTCTGGCCGTGTCTCCTGGGCAGCGTGCCTCCATCAGCTGTAGAAGCCTCCGAGAGCGTGGACAGCTACGGCTACAGCTTTATGCACTGGTATCAGCAG AGCCCGACGAGCGTGGCCACCTACTACTGCCAGCAAAGCAACGAGGATCCTTATACATTCGGCGGCGGAACCAAGCTGGAGATCAAG
10-0701-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGCAGCAATCTGGCCCTGAGCCTGTGAAGCCTGGAGCCTCTATGAAGATCAGCTGTAAAGCCAGCGGCTACACCATGAACTGGGTCAAGCAGAGCCAC GGCAAAAACCTGGAATGGATCGGCCTGATCAACCCCTATACAATGGCGGAACAACATACAACCAGAAGTTCAAGGGCAAGGCCACCCTGACCGTGGACAAGAGCAGCTCCACCGCCTACATGGAA CTGCTGTCTCTGACATCCGAGGACAGCGCCGTGTACTACTGCGCCAGAGGCCGGGGCTTATGTGGAACCCCGGATACTACGCCATGGACTACTGGGGCCAGGGCACCAGCGTGACCGTGTCCAGC
10-0701-m_VL	P2RY8 antibody light chain variable region coding sequence	CAAATCGTGCTGACACAGAGCCCTGCTATCATGAGCGCCTCTCCTGGGGAGAAGGTGACCATGACCTGTAGCGCCAGCTCTGCTCCTCCCAGCTACCTGCACTGGTACCAGCAGAAGCCTG GCAGCTCCCCTAAGCTGTGGATCTACAGCACCAGCAACCTGGCCAGCGGCGTGCCCGCCAGATTCAGCGGAAGCGGCAGCGGCACCTCTTATAGCCTGACCATCCGGAGCATGGAAGCCGAAG ACGCCGCTACATACTACTGCCACCAGTACCACAGAATCCCACTGACCTTCGGCAGCGGCACCAAGCTGGAAATCAAG
10-0716-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GACGTGCACCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCCTAGCGAGAGCCTGAGCCTCACCTGTACCGTCACCGGCTACTCCATCACCTCTGATTACGCCTGGAATTGGATCCGGCAGTTTC CAGGCAACAAGCTGGAATGGATGGGCTACGTGAGCTACTCTGGCACCACCAACATACAACCCCTCTCTGAAAAGCAGAATCAGCATCACACGGGACACCAGCAAGAACCAGTTCTTCCTGCAACT GAACAGCGTGACCACCGAGGACACCGCCACATACTTCTGCGCCAGAGGCTACTGGTACTTCGACGTGTGGGGCGCCGGCACCACCGTCACAGTGTCTGCAGC
10-0716-m_VL	P2RY8 antibody light chain variable region coding sequence	GATATCGTGCTGACACAGAGCCCCGCCTTCCTGTCCGTGACCCCTGGCGAGAAGGTGACCATCACCTGTAGCGCCAGCTCTAGCGTGACCTACATGCACTGGTATCAGCAG AGAAACCTGGCCAGAGCCCTAAGCTGTGGATCTACGCCACCAGCAACCTGGCCTCTGGCGTGCCCGCCAGATTCAGCGGCTCTGGCAGCGGCACCAGCTACAGCCTGACCATCAGCAGCATG GAGGCCGAGGACGCCGCCACCTACTACTGCCAGCAGTGGAGCAGCAACCCCCTGACCTTCGGCGCCGGCACCAAGCTGGAGCTGAAG AGCCGATGACATCGCCACATACTACTGCCAGCAAAGCAACGAGGACCCCTTCACATTCGGCAGCGGCACCCAGCTGGAAATCAAG
10-0720-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GATGTGCAGTTTCAGGAGAGCGGCCCTAGCCTGGTGAAGCCTAGCCAGAGCCTGAATCTGACCTGTACCGTCACCGGCTACTCCATCACCTCTGATTACGCCTGGAATTGGCTGAGACAGTTCC CCGGCAACAAGCTGGAATGGATGGGCTACATCAGCTACAGCGGCAACACCAACTACAACCCCAGCCTGAAAAGCAGAATCTCCATCACCAGGGACACCAGCAAGAACCAGTTCTTCCTGCAGCT GAACAGCGTGGACACCGAGGACACCGCCACATACTACTGCGCCAGAGGCTACTGGTACTTCGACGTGTGGGGAGCTGGCACAACCGTGACCGTGTCTTCT
10-0720-m_VL	P2RY8 antibody light chain variable region coding sequence	GATATCGTGCTGACCCAGAGCCCTGCTTCCCTGGCCGTGTCTCCTGGGCAGCGTGCCCACCATCAGCTGTAGAAGCGAGAGCGTGGACAGCTACGGCTACAGCTTTATGCACTGGTATCAGCAG AGAAACCTGGCCAGCCTCCAAAGCTGCTGATCTACCGGGCTTCTAATCTGGAAAGCGGCATCCCCGCTAGATTCAGCGGATCTGGCAGCAACACCAGCTTCACCCTGACAATTAACCCCGTGGA AGCCGACGACGTGGCCACATACTACTGCCAGCAAAGCAACGAGGATCCTTTCACATTCGGCGCCGGCACCAAGCTGGAGATCAAG

Table 33, Cont.

Name	Description	Sequence
10-0724-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GATGTGCAGCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCCTAGCCAGACGCTGAGCCTGACATGTACCGTCACTGGATTCTCATCACAAGCGACTACGCCTGGAATTGGATCCGGCAGTTC CCCGGCAACAAGCTGGAATGGATGGGCTACATCACCTACAGCGGCACCACGGTACAACCCAAGCCTGAAAAGCAGAATCAGCATCACGAGAATACCTCCAAGAACCACTTCTTCCTGCAAC TGTCTTCTCACCAACCGAGGACACCGCTACATACTACTGCGCCAGAGGCTTTGGTACTTGACGTGTGGGCGCCGGCACAGCCGTGACCGTGTCCAGC
10-0724-m_VL	P2RY8 antibody light chain variable region coding sequence	GATATCGTGCTGACACAGAGCCCTGCTAGCCTGGCCGTGTCCCTGGGCCAGCGGGCCACAATTTCTGTAGAGCCAGCGAGAGCGTCGACACCTACGGCTACAACTTCCTGCACTGGTATCAGC AGAAACCTGGCCAGCCTCCAAAGCTCCTGATCTACCGGGCCAGCAACCTCGCAGCGGATCCCCGCCAGATTCAGCGGCAGCGGCTCTGGCACCGACTTTACCCTGACCATCAACCCCGTGGA AGCCGACGACGTGGCCACATACTACTGCCAGCAATCCAATGAGGACCCTCCTACCATCGGCGCAGGCACCAAGCTGGAAATCAAG
10-0723-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GATGTGCAGCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCCTAGCCAGAGCCTGAGCCTGACATGTACCGTCACTGGATTCTCATCACAAGCGACTACGCCTGGAATTGGATCCGGCAGTTC CCCGGCAACAAGCTGGAATGGATGGGCTACATCACCTACAGCGGCACCACGGTACAACCCAAGCCTGAAAAGCAGAATCAGCATCACGAGAATACCTCCAAGAACCACTTCTTCCTGCAAC TGTCTTCTCACCAACCGAGGACACCGCTACATACTACTGCGCCAGAGGCTTTGGTACTTCGACGTGTGGGGCGCCGGCACAGCCGTGACCGTGTCCAGC
10-0725-m_VL	P2RY8 antibody light chain variable region coding sequence	CAAGCCGTGGTGACACAGGAATCCGCCCTCACAACAAGCCCCGGCGAAACCGTGACCCTGAGCTGTAGAAGCAGCACTGGCGCTGTGACCACCTCTAATTACGCCAACTGGCAGCAGAAA CCTGACCACTTGTTTACAGGCCTGATCGGCCACCAACAACCGGGCCCCTGGCGTGCCAGCCGGTTCTCTGGATCGGAGATAAGGCCGCCCTGACCATCACCGGCGCCCAGACCG AGGACGAGGCCATCTACTTCTGCGCCCTGTGGTACAGCAACCACTGGGTGTTCGGCGGAGGAACAAAGCTGACAGTGCTG
10-0728-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GAAGTGAAGCTTGAGGAGTCTGGAGGAGGCTTGGTCCAACCTGGAGGATCCATGAAACTCTCTTGTGCTGCCTCTGGATTCACTTTTAGTGACGCCTGGATGGACTGGGTCCGCCAGTCTCCAG AGAAGGGGCTTGAGTGGGTTGCTGAAATTAGAAGCAAAGCTAATAATCATGCAACATACTATGCTGAGTCTGTGAAAGGGAGGTTCACCATCTCAAGAGATGATTCCAAAAGTAGTGTCTACCT GCAAATGAACAGCTTAAGAGCTGAAGACACTGGCATTTATTACTGTACTGGGGACTACTGGGGCCAAGGGACCCTGGTCACTGTCTCGAGC
10-0728-m_VL	P2RY8 antibody light chain variable region coding sequence	GAAAATGTGCTCACCCAGTCTCCAGCAATCATGTCTGCATCTCTAGGGGAGAAGGTCACCATGAGCTGCAGGGCCAGCTCAAGTGTAAATTACATGTACTGGTACCAGCAGAAGTCAGATGCCT CCCCCAAACTATGGATTTATACACATCCAACCTGGCTCCTGGAGTCCCAGCTTCAGTGGCAGTGGGTCTGGGAACTCTTATTCTCTCACAATCAGCAGCATGGAGGCTGAAGATGCTGCC ACTTATTACTGCCAGCAGTTTACTAGTTCCCCGTACACGTTCGGAGGGGGCACCAAGCTGGAAATAAAA
10-0729-m_VH	P2RY8 antibody heavy chain variable region coding sequence	GATGTGCTAGCTGCAGGAGAGCGGACCTGGCCTGGTGAAGCCTCAGCCACAGAGCCTGAGCCTGACCTGTACCGTGACTGGCTACAGCATCACAAGCGACTTCGCCTGGAACTGGATCCGGCAGGGT GCCAGGGCAACAAGCTGGAATGGATGGGCTATATCTCCTACTCTGGCACCACCAGATACAACCCTAGCCTGAAGTCCAGAATCTCTATCACCCGGGACACCAGCAAGAACCAGTTCTTCCTGCAAC TCAACAGCGTGACCCCTGAGGATACCGCCACATACTACTGCGCCAGAGGCTACTGGTACTTCGACGTGTGGGGCGCTGGAACAACAGTCACAGTGTCTCCAGC
10-0729-m_VL	P2RY8 antibody light chain variable region coding sequence	GATATCGTGCTGACACAATCTCCAGCTAGCCTGGCCGTGTCCCTGGGCCAGCGGGCCACAATCAGCTGTAGAGCCAGCGAGAGCGTCGACAACTACGGCTACAGCTTTATGCACTGGTATCAGC ACAAACCTGGCCAGCCTCCCAAGCTGCTGATCTACCGGGCCAGCAACCTGGAAAGCGGGATCCCCGCCAGATTCAGCGGCAGCGGCTCTAGAACCGACTTCACCCTGACCATCAACCCCGTGGA AGCCGACGATGTGGCCACCTACTACTGCCAGCAGAGCAACGAGGACCCTCTTACACCTTCGGCGGCGGCACCAAGCTGGAGATCAAG

Table 34: Exemplary nucleic acid sequence encoding humanized VH and humanized VL of humanized P2RY8 antibodies



Name	Description	Sequence
10-0716-h1_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCATCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCCCGGCAAAGGGCCTGGAGTGGGTGGCCTACATCACCTACAGCGGCAACACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCAGGGACACCAGCAAGAACCAGTTCTACCTGCA AGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h1_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGGGCGTGAGCACCTACGTGACCTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGGCGCCAGCAACAGGTACACCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCT TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGACAACGAGGACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
10-0716-h2_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCATCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCCCGGCAAAGGGCCTGGAGTGGGTGGCCTACATCACCTACAGCGGCAACACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCAGGGACACCAGCAAGAACCAGTTCTACCTGCA AGATGAACAGCCTGAGGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h2_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGGGCGTGAGCACCTACGTGACCTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGGCGCCAGCAACAGGTACACCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCT TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGACAACGAGGACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
10-0716-h3_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCATCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCCCGGCAAAGGGCCTGGAGTGGGTGGCCTACATCACCTACAGCGGCAACACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCAGGGACACCAGCAAGAACCAGTTCTACCTGCA AGCTGAACAGCGTGTCGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h3_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGGGCGTGAGCACCTACGTGACCTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGGCGCCAGCAACAGGTACACCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCT TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGACAACGAGGACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
10-0716-h4_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTTCACCATCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCCCGGCAAAGGGCCTGGAGTGGGTGGCCTACATCACCTACAGCGGCAACACCAACTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACCAGTTCTACCTGCA AGCTGAACAGCGTGACCGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h4_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGGGCGTGAGCACCTACGTGACCTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGGCGCCAGCAACAGGTACACCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCT TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGACAACGAGGACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
10-0716-h5_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCATCAGCGACTACGCCTGGAACTGGATCAGGCAGGCC CCCCCGGCAAAGGGCCTGGAGTGGGTGGCCTACATCACCTACAGCGGCAACACCAACTACAACCCCAGCCTGAAGAGCAGGGTGACCATCAGCAGGGACACCAGCAAGAACCAGTTCTACCTGCA AGCTGAACAGCGTGTCGGCCGAGGACACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h5_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGGGCGTGAGCACCTACGTGACCTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGGCGCCAGCAACAGGTACACCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCT TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGACAACGAGGACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 34, Cont.

Name	Description	Sequence
19-0716-h6_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGACAGCGGCGGCGGCGTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGACAGGCTACACCATCACCAGCGACTACGCCTGGAACTGGATCAGGCAGG CCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAGCGGCACCACCACCTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACCAGTTCTACCTGC AGCTGAACAGCGTGACAGCCGCGGACACCGCCGTGTACTACTGCGTGAGCGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCCTGGTCACCGTGAGCAGC
19-0716-h6_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGCGCCAGCCTGAGCAGCGTGAGCTACATGCACTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGACCAGCAACCTGGCGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCC TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGGCAACGAGCTTCCCTACACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
19-0716-h8_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGACCGGCGGCGGCCTGGTGCAGCCCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTACGCCTTCACCAGCTACTGGATCGGCTGGGTGAGGCAGG CCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCTACCCCGGCGACAGCGACACCAGATACAGCCCCAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCC AGCCTGAACGCCAGCGACACCGCCATGTACTACTGCGCCAGGCACGTGGACTACTGGGGCCAGGGCACCCTGGTCACCGTGAGCGCC
19-0716-h8_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGCGCCAGCCTGAGCAGCGTGAGCTACATGCACTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGACCAGCAACCTGGCCAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCC TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGGCAACGAGCTTCCCTACACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
19-0724-h3_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTACGCCTTCACCAGCTACTGGATCGGCTGGGTGAGGCAGG CCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCTACCCCGGCGACAGCGACACCAGATACAGCCCCAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCC AGCCTGAACGCCAGCGACACCGCCATGTACTACTGCGCCAGGCACGTGGACTACTGGGGCCAGGGCACCCTGGTCACCGTGAGCGCC
19-0724-h3_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGCGCCAGCCTGAGCAGCGTGAGCTACATGCACTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGACCAGCAACCTGGCCAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCC TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGGCAACGAGCTTCCCTACACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
19-0724-h4_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGACAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTACGCCTTCACCAGCTACTGGATCGGCTGGGTGAGGCAGG CCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCTACCCCGGCGACAGCGACACCAGATACAGCCCCAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCC AGCCTGAACGCCAGCGACACCGCCATGTACTACTGCGCCAGGCACGTGGACTACTGGGGCCAGGGCACCCTGGTCACCGTGAGCGCC
19-0724-h4_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGCGCCAGCCTGAGCAGCGTGAGCTACATGCACTGGTACCA CAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGACCAGCAACCTGGCCAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCC GCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGGCAACGAGCTGCCCTACACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
19-0724-h5_VH	P2RY8 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGACAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTACGCCTTCACCAGCTACTGGATCGGCTGGGTGAGGCAGG CCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCTACCCCGGCGACAGCGACACCAGATACAGCCCCAGCTTCCAGGGCCAGGTGACCATCAGCGCCGACAAGAGCATCAGCACCGCC AGCTGAACAGCGTGACAGCCGCGGACACCGCCGTGTACTACTGCGTGAGCGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCCTGGTCACCGTGAGCAGC
19-0724-h5_VL	P2RY8 antibody light chain variable region coding sequence	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGCGCCAGCCTGAGCAGCGTGAGCTACATGCACTGGTACCA GCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGACCAGCAACCTGGCCAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCC TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGGGCAACGAGCTTCCCTACACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 34, Cont.

Name	Description	Sequence
10-0724-h6_VH	P2R18 antibody heavy chain variable region coding sequence	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCTGGCAGGAGCCTGAGACTGAGCTGCGCCGCCAGCGGCTTCACCTTCGACGACTACGCCATGCACTGGGTCAGACAGGCCCCTGGCAAGGGCCTGGAATGGGTGAGCGGCATCACCTGGAACAGCGGCCACATCGACTACGCCGACAGCGTGGAAGGCAGATTCACCATCAGCCGGGACAACGCCAAGAACAGCCTGTACCTGCAGATGAACAGCCTGAGAGCCGAGGACACCGCCGTGTACTACTGCGCCAAGGTGAGCTACCTGAGCACCGCCAGCAGCCTGGACTACTGGGGCCAGGGCACCCTGGTGACCGTGAGCAGC
10-0724-h6_VL	P2R18 antibody light chain variable region coding sequence	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGAGTGACCATCACCTGCAGAGCCAGCGAGAGCGTGGACAACTACGGCATCAGCTTCATGAACTGGTTCCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCGCCAGCAACCAGGGCAGCGGCGTGCCCAGCAGATTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTACTGCCAGCAGAGCAAGGAGGTGCCCTACACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 35: Exemplary nucleic acid sequence encoding human Ig light chain constant regions, kappa (IGKC) and lambda 2 (IGLC2), and human Ig heavy chain constant region, gamma 1 (IGHG1), of humanized P2RY8 antibodies

Name	Description	Sequence
Human Immunoglobulin kappa constant (IGKC)	Nucleic acid encoding human immunoglobulin light chain kappa constant region (Uniprot ID: P01834) for human IgG1 expression	CGTACGGTGGCGGCGCCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGT TGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCG GGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGAC GCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCC CGTCACAAAGAGCTTCAACAGGGGAGAGTGTTAG
Human Immunoglobulin lambda constant 2 (IGLC2)	Nucleic acid encoding human immunoglobulin light chain lambda constant 2 region (Uniprot ID: P0DOY2) for human IgG1 expression	GGTCAGCCCAAGGCGGCGCCCTCGGTCACTCTGTTCCCGCCCTCCTCTGAGGAGCTTCAAGCCAACAAGGCC ACACTGGTGTGTCTCATAAGTGACTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGGCAGATAGCAGCCCC GTCAAGGCGGGAGTGGAGACAACCACACCCTCCAAACAAAGCAACAACAAGTACGCGGCCAGCTATCT GAGCCTGACGCCTGAGCAGTGGAAGTCCCACAGAAGCTACAGCTGCCAGGTCACGCATGAAGGGAGCACCG TGGAGAAGACAGTGGCCCCTACAGAATGTTCATAG

Table 35, Cont.

Name	Description	Sequence
Human immunoglobulin heavy constant gamma 1 (IGHG1)	Nucleic acid encoding human immunoglobulin heavy gamma 1 constant region (Uniprot ID: P01857) for human IgG1 expression	GCTAGCACCAAGGGCCCATCGGTCTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTGGGGGCACAGCGGCC CTGGGCTGCCTGGTCAAGGACTACTTCCCCGAACCGGTGACGGTGTCGTGGAACTCAGGCGCCCTGACCAGC GGCGTGCACACCTTCCCGGCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAGCAGCGTGGTGACCGTGCCCT CCAGCAGCTTGGGCACCCAGACCTACATCTGCAACGTGAATCACAAGCCCAGCAACACCAAGGTGGACAAGA AAGTTGAGCCCAAATCTTGTGACAAAACTCACACATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGGGACC GTCAGTCTTCCTCTTCCCCCCAAAACCCAAGGACACCCTCATGATCTCCCGGACCCCTGAGGTCACATGCGTGG TGGTGGACGTGAGCCACGAAGACCCTGAGGTCAAGTTCAACTGGTACGTGGACGGCGTGGAGGTGCATAAT GCCAAGACAAAGCCGCGGGAGGAGCAGTACAACAGCACGTACCGTGTGGTCAGCGTCCTCACCGTCCTGCAC CAGGACTGGCTGAATGGCAAGGAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAGAAA ACCATCTCCAAAGCCAAAGGGCAGCCCCGAGAACCACAGGTGTACACCCTGCCCCCATCCCGGGATGAGCTG ACCAAGAACCAGGTCAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGGAGTGGGAG AGCAATGGGCAGCCGGAGAACAACTACAAGACCACGCCTCCCGTGCTGGACTCCGACGGCTCCTTCTTCCTCT ACAGCAAGCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTCCGTGATGCATGAG GCTCTGCACAACCACTACACGCAGAAGAGCCTCTCCCTGTCTCCGGGTAAATGA

Table 36: Exemplary nucleic acid sequence encoding mouse V_H, mouse V_L, and CDR sequences of chimeric P2RY8 antibodies

Name of VH or VL, CDR annotation	Antibodies	Sequence CDR for VH or VL
10-0690-m_VH	**10-0690-m**	
10-0690-m_VH - IMGT_CDR1		GGCTATAGCATCACCTCTGATTACGCC
10-0690-m_VH - IMGT_CDR2		ATCGACTACAGCGGCAGCACC
10-0690-m_VH - IMGT_CDR3		ACCAGAGGCTTCTGGTACTTCGACGTG
10-0690-m_VL	p10-0690-m	
10-0690-m_VL - IMGT__CDR1		GAAAGCGTGGACAGCTACGGCTACACCTTT
10-0690-m_VL - IMGT__CDR2		CGGGCTTCT
10-0690-m_VL - IMGT_CDR3		CAGCAGAGCAACGAGGATCCTTTCACC
10-0695-m_VH	**10-0695-m**	
10-0695-m_VH - IMGT_CDR1		GGCTACAGCATCACCTCTGATTACGCC
10-0695-m_VH - IMGT_CDR2		ATCTCTTATAGCGGCAGCACC
10-0695-m_VH - IMGT_CDR3		GCCAGAGGCTACTGGTACTTCGACGTG
10-0695-m_VL	10-0695-m	
10-0695-m_VL - IMGT__CDR1		GAGAGCGTCGACAGCTACGGCTACAGCTTT
10-0695-m_VL - IMGT__CDR2		CGGGCCTCT
10-0695-m_VL - IMGT_CDR3		CAGCAAAGCAACGAGGATCCTTATACA
10-0701-m_VH	**10-0701-m**	
10-0701-m_VH - IMGT_CDR1		AGCAGCAGCTTCACCGGCTACACC
10-0701-m_VH - IMGT_CDR2		ATCAACCCATACAATGGCGGAACA
10-0701-m_VH - IMGT_CDR3		GCCAGAGGCCGGGCTTATGTGAACCCCGGAGATTACGCCATGGACTAC
10-0701-m_VL	10-0701-m	
10-0701-m_VL - IMGT_CDR1		AGCTCTGCCTCCTCCAGCTAC
10-0701-m_VL - IMGT_CDR2		AGCACCAGC
10-0701-m_VL - IMGT_CDR3		CACCAGTACCACAGATCTCCATACACC

Table 36, Cont.

Name of VH or VL, CDR annotation	Antibodies	Sequence CDR for VH or VL
10-0716-m_VH	**10-0716-m**	
10-0716-m_VH - IMGT_CDR1		GCCTACTCCATCACCTCTGATTACGCC
10-0716-m_VH - IMGT_CDR2		GTGACCTACTCTGGCACCACA
10-0716-m_VH - IMGT_CDR3		GCCAGAGGCTACTGGTACTTCGACGTG
10-0716-m_VL	10-0716-m	
10-0716-m_VL - IMGT__CDR2		CGGGCCTCT
10-0716-m_VL - IMGT_CDR1		GAGAGCGTCGACAGCTACGGCTACACCTTT
10-0716-m_VL - IMGT_CDR3		CAGCAAAGCAACGAGGACCCCTTCACA
10-0720-m_VH	**10-0720-m**	
10-0720-m_VH - IMGT_CDR1		GGCTATAGCATCACCTCTGATTACGCC
10-0720-m_VH - IMGT_CDR2		ATCAGCTACAGCGGCACCACA
10-0720-m_VH - IMGT_CDR3		GCCAGAGGCTACTGGTACTTCGACGTG
10-0720-m_VL	10-0720-m	
10-0720-m_VL - IMGT_CDR1		GAGAGAGTGGACAGCTACGGCTACACCTTT
10-0720-m_VL - IMGT_CDR2		CGGGCCTCT
10-0720-m_VL - IMGT_CDR3		CAGCAAAGCAACGAGGATCCTTTCACA
10-0724-m_VH	**10-0724-m**	
10-0724-m_VH - IMGT_CDR1		GGATATTCTATCACAAGCGACTACGCC
10-0724-m_VH - IMGT_CDR2		ATCACCTACAGCGGCACCACA
10-0724-m_VH - IMGT_CDR3		GCCAGAGGCTTTTGGTACTTCGACGTG
10-0724-m_VL	10-0724-m	
10-0724-m_VL - IMGT_CDR1		GAGAGCGTCGACACCTACGGCTACAACTTC
10-0724-m_VL - IMGT_CDR2		CGGGCCAGC
10-0724-m_VL - IMGT_CDR3		CAGCAATCCAATGAGGACCTGCTGACC

Table 36, Cont.

Name of VH or VL, CDR annotation	Antibodies	Sequence CDR for VH or VL
10-0725-m_VH	**10-0725-m**	
10-0725-m_VH - IMGT_CDR1		GGATATTCTATCACAAGCGACTACGCC
10-0725-m_VH - IMGT_CDR2		ATCACCTACAGCGGCACCACA
10-0725-m_VH - IMGT_CDR3		GCCAGAGGCTTTTGGTACTTCGACGTG
10-0725-m_VL	10-0725-m	
10-0725-m_VL - IMGT_CDR1		ACCGGCGCTGTGACCACCTCTAATTAC
10-0725-m_VL - IMGT_CDR2		GGCACCAAC
10-0725-m_VL - IMGT_CDR3		GCCCTGTGGTACAGCAACCACTGGGTG
10-0728-m_VH	**10-0728-m**	
10-0728-m_VH - IMGT_CDR1		GGATTCACTTTTAGTGACGCCTGG
10-0728-m_VH - IMGT_CDR2		ATTAGAAGCAAAGCTAATAATCATGCAACA
10-0728-m_VH - IMGT_CDR3		ACGGGTTTTATGATTACGACGGCCTGGTTTGCTTAC
10-0728-m_VL	10-0728-m	
10-0728-m_VL - IMGT_CDR1		TCAAGTGTAAATTAC
10-0728-m_VL - IMGT_CDR2		TACACATCC
10-0728-m_VL - IMGT_CDR3		CAGCAGTTTACTAGTTCCCCGTACACG
10-0729-m_VH	**10-0729-m**	
10-0729-m_VH - IMGT_CDR1		GGCTACAGCATCACAAGCGACTTCGCC
10-0729-m_VH - IMGT_CDR2		ATCTCCTACTCTGGCACCACC
10-0729-m_VH - IMGT_CDR3		GCCAGAGGCTACTGGTACTTCGACGTG
10-0729-m_VL	10-0729-m	
10-0729-m_VL - IMGT_CDR1		GAGAGCGTCGACAGCTACGGCTACACCTTT
10-0729-m_VL - IMGT_CDR2		CGGGCCTCT
10-0729-m_VL - IMGT_CDR3		CAGCAGAGCAACGACGATCCTTACACC

Table 37: Exemplary nucleic acid sequence encoding humanized V_H, humanized V_L, CDR, and FR sequences of humanized P2RY8 antibodies

Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0716-h1_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCTGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTACAGCATCACC
		AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGGCTACATCACCTACAGCGGCACCACCACCTAC
		AACCCCAGCCTGAAGAGCAGGGTTACCATCAGCAGGGACACCAGGAAGAACACCCTGTACCTGCAGATGAACAGCCTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0716-h1_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0716-h1_VH - IMGT_CDR2	ATCACCTACAGCGGCACCACC
	10-0716-h1_VH - IMGT_CDR3	GCCAGGGGCTACTGGTACTTCGACGTG
	10-0716-h1_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCTGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGC
	10-0716-h1_VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGGCTAC
	10-0716-h1_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCAGGGTTACCATCAGCAGGGACACCAGGAAGAACACCCTGTACCTGCAGATGAACAGCCTGAGGGCC
	10-0716-h1_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h1_VL		GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC
		AGCTACGGCTACAGCTTCATGCACTGGTACCAGCAGAAGCCCGGCCAAGCCCCCCAAGCTGCTGATCTACAGGGCCAACGTGGAGAGC
		GGCGTGCCCGACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACT
	10-0716-h1_VL - IMGT_CDR1	GAGAGCGTGGACAGCTACGGCTACAGCTTC
	10-0716-h1_VL - IMGT_CDR2	AGGGCCAGC
	10-0716-h1_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCCCTTCACC
	10-0716-h1_VL - IMGT_FR1	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGC
	10-0716-h1_VL - IMGT_FR2	ATGCACTGGTACCAGCAGAAGCCCGGCCAAGCCCCCCAAGCTGCTGATCTAC
	10-0716-h1_VL - IMGT_FR3	AACGTGGAGAGCGGCGTGCCCGACAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC
	10-0716-h1_VL - IMGT_FR4	TTCGCCACCTACTTCTGCCAGCAGAGCAACGAGGACCCCTTCACCTTCGGCCAAGGGACCAAGGTGGAGATCAAG

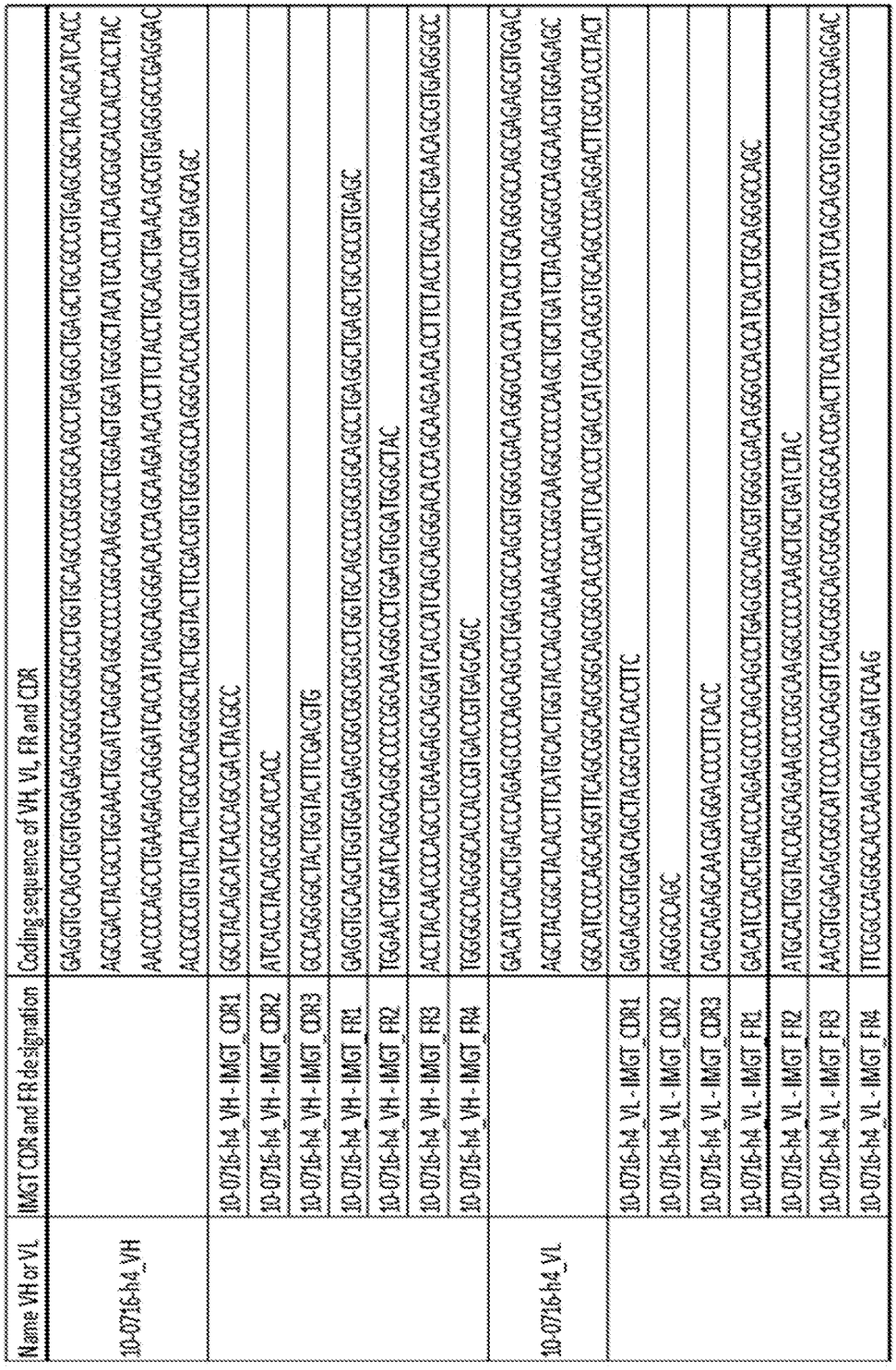
Table 37, Cont.

Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
1D-0716-h2_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTTCAGCATCACC
		AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGGCTACATCACCTACAGCGGCAACCACCACCTAC
		AACCCCAGCCTGAAGAGCAGGTTCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGATGAACAGCCTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	1D-0716-h2_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	1D-0716-h2_VH - IMGT_CDR2	ATCACCTACAGCGGCAACCACC
	1D-0716-h2_VH - IMGT_CDR3	GCCAGGGGCTACTGGTACTTCGACGTG
	1D-0716-h2_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGC
	1D-0716-h2_VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGGCTAC
	1D-0716-h2_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCAGGTTCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGATGAACAGCCTGAGGGCC
		GAGGACACCGCCGTGTACTACTGC
	1D-0716-h2_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
1D-0716-h2_VL		GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGGACGTGGAC
		AGCTACGGCTACACCTTCATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACGCCAACGTGGAGAGC
		GGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACT
	1D-0716-h2_VL - IMGT_CDR1	GAGAGCGTGGAGACAGCTACGGCTACACCTTC
	1D-0716-h2_VL - IMGT_CDR2	AGCGCCAGC
	1D-0716-h2_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCCTTCACC
	1D-0716-h2_VL - IMGT_FR1	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGC
	1D-0716-h2_VL - IMGT_FR2	ATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	1D-0716-h2_VL - IMGT_FR3	AACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC
		TTCGCCACCTACTACTGC
	1D-0716-h2_VL - IMGT_FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.

Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0716-h3_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCCTGGTGCAGCCTGGGGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTACACCATCACC
		AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCTGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAGCGGCACCACCTAC
		AACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCCTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0716-h3_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0716-h3_VH - IMGT_CDR2	ATCACCTACAGCGGCACCACC
	10-0716-h3_VH - IMGT_CDR3	GCCAGGGGCTACTGGTACTTCGACGTG
	10-0716-h3_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCCTGGTGCAGCCTGGGGGCAGCCTGAGACTGAGCTGCGCCGTGAGC
	10-0716-h3_VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCTGGCAAGGGCCTGGAGTGGATGGGCTAC
	10-0716-h3_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCCTCTACCTGCAGCTGAACAGCGTGAGGGCC
	10-0716-h3_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h3_VL		GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC
		AGCTACGGCTACACCTTCATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAGCAACGTGGAGAGC
		GGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACT
	10-0716-h3_VL - IMGT_CDR1	GAGAGCGTGGACAGCTACGGCTACACCTTC
	10-0716-h3_VL - IMGT_CDR2	AGGGCCAGC
	10-0716-h3_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCCTTCACC
	10-0716-h3_VL - IMGT_FR1	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGC
	10-0716-h3_VL - IMGT_FR2	ATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0716-h3_VL - IMGT_FR3	AACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC
	10-0716-h3_VL - IMGT_FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.



Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0716-h4_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTACAGCATCACC
		AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGGCTATCACCTACAGCGGCACCACCTAC
		AACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0716-h4_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0716-h4_VH - IMGT_CDR2	ATCACCTACAGCGGCACCAC
	10-0716-h4_VH - IMGT_CDR3	GCCAGGGGCTACTGGTACTTCGACGTG
	10-0716-h4_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGC
	10-0716-h4_VH - IMGT_FR2	TGGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGGTGGCTAC
	10-0716-h4_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCC
	10-0716-h4_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h4_VL		GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC
		AGCTACGGCTACAGCTTCATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAGCAACGTGGAGAGC
		GGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCGTGCAGCCCGAGGACTTCGCCACCTACT
	10-0716-h4_VL - IMGT_CDR1	GAGAGCGTGGACAGCTACGGCTACAGCTTC
	10-0716-h4_VL - IMGT_CDR2	AGGGCCAGC
	10-0716-h4_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCCTTCACC
	10-0716-h4_VL - IMGT_FR1	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGC
	10-0716-h4_VL - IMGT_FR2	ATGGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0716-h4_VL - IMGT_FR3	AACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCGTGCAGCCCGAGGAC
	10-0716-h4_VL - IMGT_FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.

Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0716-h5_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTACAGCATCACC AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAGCGGCACCACCACCTAC AACCCCAGCCTGAAGAGCCAGGTGACCATCAGCGTGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC ACCGCCGTGTACTACTGCGCCAGCGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0716-h5_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0716-h5_VH - IMGT_CDR2	ATCACCTACAGCGGCACCACC
	10-0716-h5_VH - IMGT_CDR3	GCCAGCGGCTACTGGTACTTCGACGTG
	10-0716-h5_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCTGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGC
	10-0716-h5_VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATGGGCTAC
	10-0716-h5_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCCAGGTGACCATCAGCGTGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCC GAGGACACCGCCGTGTACTACTGC
	10-0716-h5_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h5_VL		GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC AGCTACGGCTACACCTTCATGCACTGGTACCAGCAGAAGCCCGGCCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAGCAACGTGGAGAGC GGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCAGGGACCGGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACT
	10-0716-h5_VL - IMGT_CDR1	GAGAGCGTGGACAGCTACGGCTACACCTTC
	10-0716-h5_VL - IMGT_CDR2	AGGGCCAGC
	10-0716-h5_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCCTTCACC
	10-0716-h5_VL - IMGT_FR1	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGC
	10-0716-h5_VL - IMGT_FR2	ATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0716-h5_VL - IMGT_FR3	AACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCAGGGACCGGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC TTCGCCACCTACTAC TGC
	10-0716-h5_VL - IMGT_FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

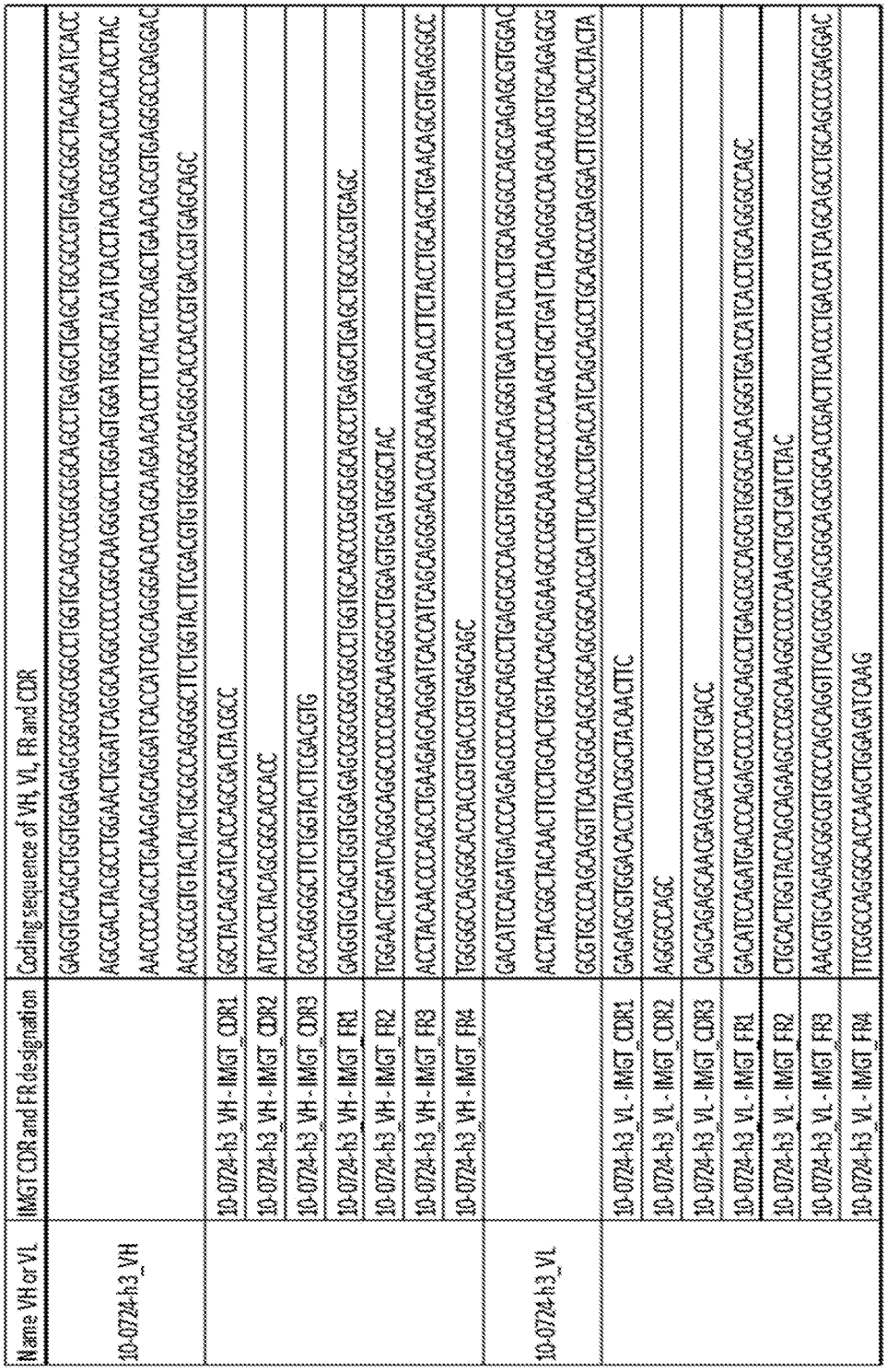
Table 37, Cont.

Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0716-h6_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTACAGCATCACC AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATGGGCTACATCACCTACAGCGGCAGCACCACCTAC AACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC ACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0716-h6 VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0716-h6 VH - IMGT_CDR2	ATCACCTACAGCGGCAGCACC
	10-0716-h6 VH - IMGT_CDR3	GCCAGGGGCTACTGGTACTTCGACGTG
	10-0716-h6 VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGC
	10-0716-h6 VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATGGGCTAC
	10-0716-h6 VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h6_VL		GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC AGCTACGGCTACACCTTCATGCACTGGTACCAGCAGAAGCCCGGCCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAGCAACGTGGAGAGC GGCATCCCCAGCAGGTTCAGCGGCAGCGGCAGCAGGGACCGACTTCACCCTGACCATCAGCAGGCTGCAGCCCGAGGACTTCGCCACCTACT ACTGCCAGCAGAGCAACGAGGACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAGATCAAG
	10-0716-h6_VL - IMGT_CDR1	GAGAGCGTGGACAGCTACGGCTACACCTTC
	10-0716-h6_VL - IMGT_CDR2	AGGGCCAGC
	10-0716-h6_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCCTTCACC
	10-0716-h6_VL - IMGT_FR1	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGC
	10-0716-h6_VL - IMGT_FR2	ATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0716-h6_VL - IMGT_FR3	AACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC TTCGCCACCTACTACTGC
	10-0716-h6_VL - IMGT_FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.

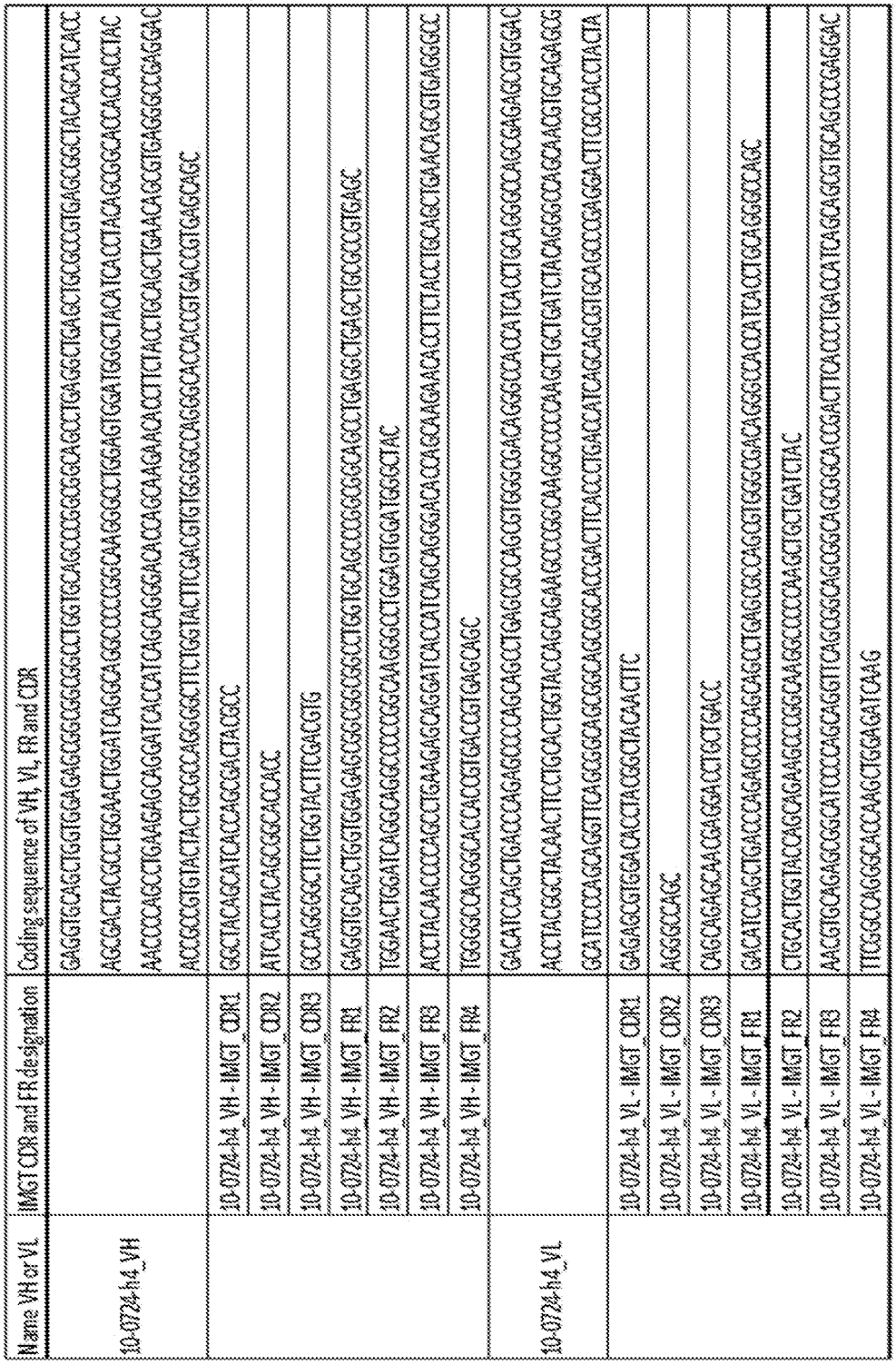
Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0716-h8_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTACAGCATCACC
		AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATTGGGCTACATCACCTACAGCGGCACCACCTAC
		GCCGACAGCCTGAAGGGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTACTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0716-h8 VH - IMGT CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0716-h8 VH - IMGT CDR2	ATCACCTACAGCGGCACCACC
	10-0716-h8 VH - IMGT CDR3	GCCAGGGGCTACTGGTACTTCGACGTG
	10-0716-h8 VH - IMGT FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGC
	10-0716-h8 VH - IMGT FR2	TGGGTGCGCCAGGCCCCCGGCAAGGGCCTGGAGTGGATTGGGCTAC
	10-0716-h8 VH - IMGT FR3	ACCTACAGCGGCACCACCTACTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCC
	10-0716-h8 VH - IMGT FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0716-h8_VL		GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC
		AGCTACGGCTACACCTTCATGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAGCAACGTGGAGAGC
		GGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACT
	10-0716-h8 VL - IMGT CDR1	GAGAGCGTGGACAGCTACGGCTACACCTTC
	10-0716-h8 VL - IMGT CDR2	AGGGCCAGC
	10-0716-h8 VL - IMGT CDR3	CAGCAGAGCAACGAGGACCCCTTCACC
	10-0716-h8 VL - IMGT FR1	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGC
	10-0716-h8 VL - IMGT FR2	ATGGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0716-h8 VL - IMGT FR3	AACGTGGAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC
	10-0716-h8 VL - IMGT FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.



Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0724-h3_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGCGGCTACAGCATCACC
		AGCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATTGGCTACATCACCTACAGCGGCACCACCACCTAC
		AACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTTCTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0724-h3_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0724-h3_VH - IMGT_CDR2	ATCACCTACAGCGGCACCACC
	10-0724-h3_VH - IMGT_CDR3	GCCAGGGGCTTCTGGTACTTCGACGTG
	10-0724-h3_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTTGGTGCAGCCCGGCGGCAGCCTGAGGCTGAGCTGCGCCGTGAGC
	10-0724-h3_VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATTGGCTAC
	10-0724-h3_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCC
	10-0724-h3_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0724-h3_VL		GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC
		ACCTACGGCTACAACTTCCTGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAGCAACCTGGAAAGC
		GCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGACTTCGCCACCTACTA
	10-0724-h3_VL - IMGT_CDR1	GAGAGCGTGGACACCTACGGCTACAACTTC
	10-0724-h3_VL - IMGT_CDR2	AGGGCCAGC
	10-0724-h3_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCTGCTGACC
	10-0724-h3_VL - IMGT_FR1	GACATCCAGATGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGTGACCATCACCTGCAGGGCCAGC
	10-0724-h3_VL - IMGT_FR2	CTGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0724-h3_VL - IMGT_FR3	AACGTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC
	10-0724-h3_VL - IMGT_FR4	TTCGGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.

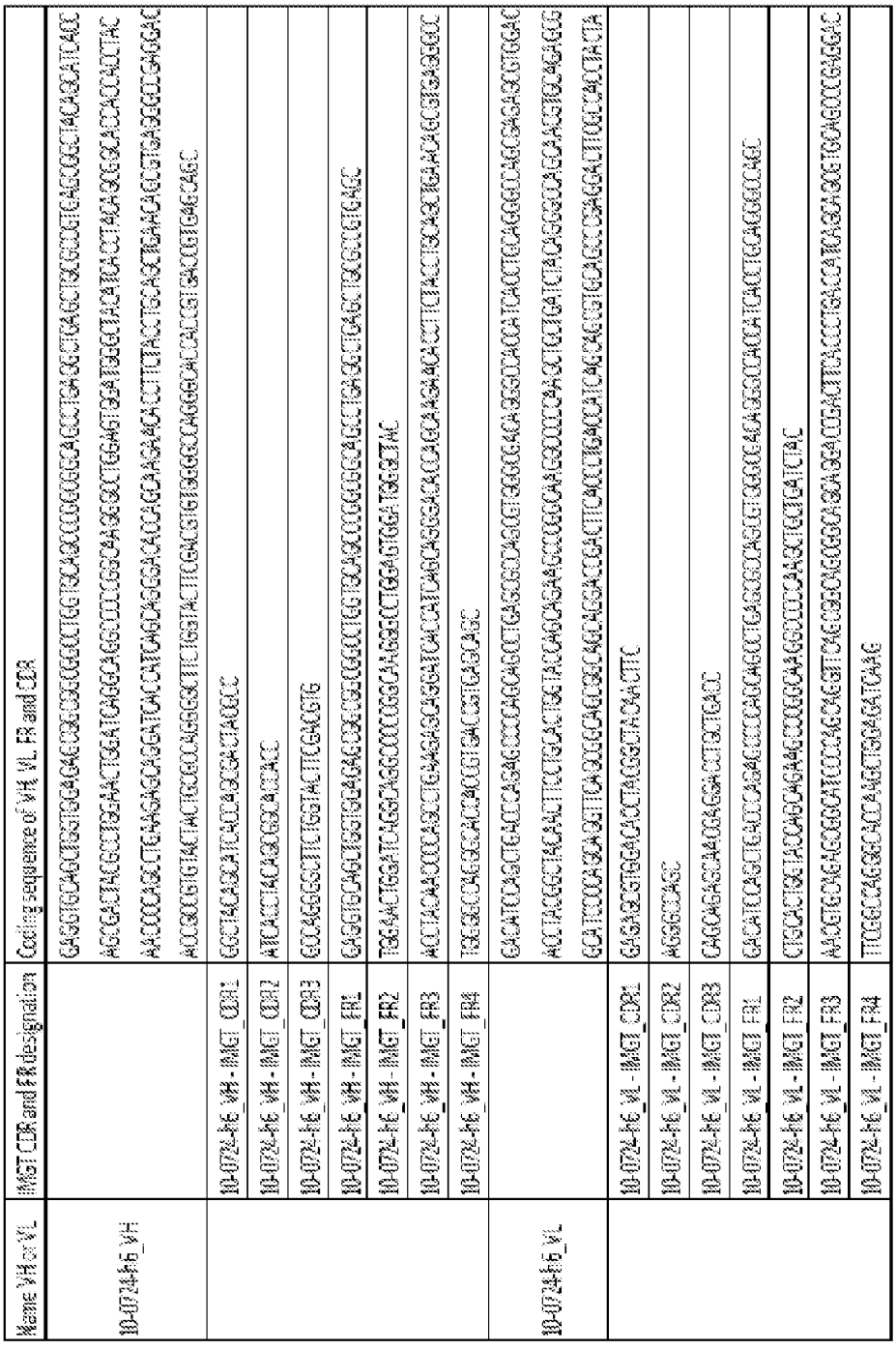


Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-0724-h4_VH		GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCTGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGCGGCTACAGCATCACC
		ACCGACTACGCCTGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATTGGCTACATCACCTACAGCGGCACCACCTAC
		AACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCCGAGGAC
		ACCGCCGTGTACTACTGCGCCAGGGGCTTCTGGTACTTCGACGTGTGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
	10-0724-h4_VH - IMGT_CDR1	GGCTACAGCATCACCAGCGACTACGCC
	10-0724-h4_VH - IMGT_CDR2	ATCACCTACAGCGGCACCACC
	10-0724-h4_VH - IMGT_CDR3	GCCAGGGGCTTCTGGTACTTCGACGTG
	10-0724-h4_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGAGCGGCGGCGGCCTGGTGCAGCCTGGCGGCAGCCTGAGACTGAGCTGCGCCGTGAGC
	10-0724-h4_VH - IMGT_FR2	TGGAACTGGATCAGGCAGGCCCCCGGCAAGGGCCTGGAGTGGATTGGCTAC
	10-0724-h4_VH - IMGT_FR3	ACCTACAACCCCAGCCTGAAGAGCAGGATCACCATCAGCAGGGACACCAGCAAGAACACCTTCTACCTGCAGCTGAACAGCGTGAGGGCC
	10-0724-h4_VH - IMGT_FR4	TGGGGCCAGGGCACCACCGTGACCGTGAGCAGC
10-0724-h4_VL		GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGCGAGAGCGTGGAC
		ACCTACGGCTACAACTTCCTGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTACAGGGCCAACGTGCAGAGCGG
		CGTACCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCGTGCAGCCCGAGGACTTCGCCACCTACTA
	10-0724-h4_VL - IMGT_CDR1	GAGAGCGTGGACAACTACGGCTACGAACTTC
	10-0724-h4_VL - IMGT_CDR2	AGGGCCAGC
	10-0724-h4_VL - IMGT_CDR3	CAGCAGAGCAACGAGGACCCTCGTGACC
	10-0724-h4_VL - IMGT_FR1	GACATCCAGCTGACCCAGAGCCCCAGCAGCCTGAGCGCCAGCGTGGGCGACAGGGCCACCATCACCTGCAGGGCCAGC
	10-0724-h4_VL - IMGT_FR2	CTGCACTGGTACCAGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGATCTAC
	10-0724-h4_VL - IMGT_FR3	AACGTGCAGAGCGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCGACTTCACCCTGACCATCAGCAGCCTGCAGCCCGAGGAC
	10-0724-h4_VL - IMGT_FR4	TTCGCCACCTACTTCTGCCAGGGCACCAAGCTGGAGATCAAG

Table 37, Cont.

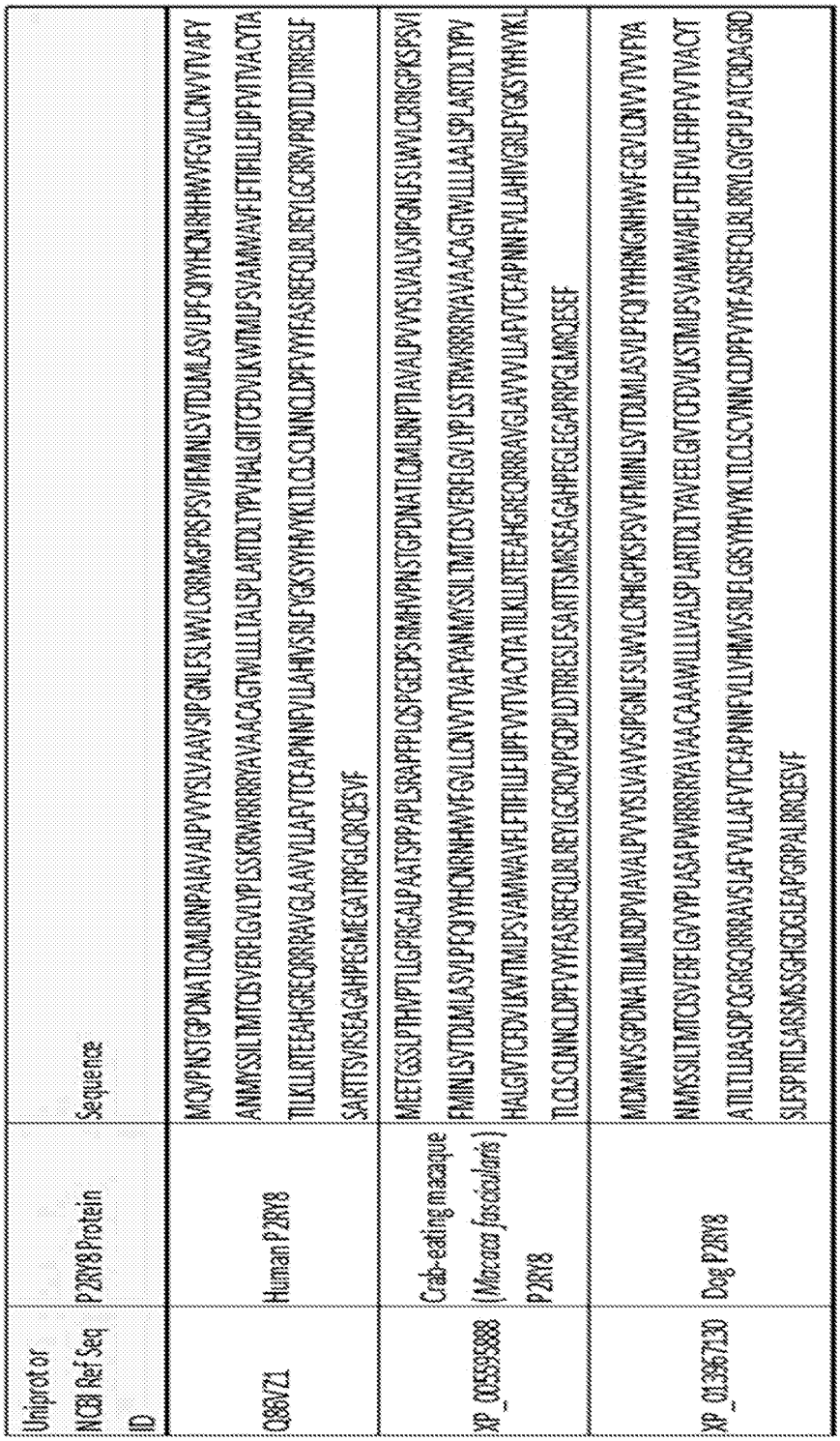
Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL, FR and CDR
10-D724-h5_VH		GAGGTGCAGCTGGTGGAGACTGGAGGAGGCTTGATCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGTAGCTATGCTATGAGCTGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCAGCTATTAGTGGTAGTGGTGGTAGCACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAAGATCGGGCCTACTATGATTTTTGGAGTGGTTATTATAACTACTACTACGGTATGGACGTCTGGGGCCAAGGGACCACGGTCACCGTCTCCTCAG
	10-D724-h5_VH - IMGT_CDR1	GGCTACAGCATCACCAGTGGTTATAGCTGC
	10-D724-h5_VH - IMGT_CDR2	ATCACCTACAGCGGCACCACC
	10-D724-h5_VH - IMGT_CDR3	GCCAGGGGCTTCTGGTACTTCGATCTC
	10-D724-h5_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGACTGGAGGAGGCTTGATCCAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAGCCTCTGGATTCACCTTTAGT
	10-D724-h5_VH - IMGT_FR2	TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGTGGGTCTCA
	10-D724-h5_VH - IMGT_FR3	AGTACATACTACGCAGACTCCGTGAAGGGCCGGTTCACCATCTCCAGAGACAATTCCAAGAACACGCTGTATCTGCAAATGAACAGCCTGAGAGCCGAGGACACGGCCGTATATTACTGTGCGAAA
	10-D724-h5_VH - IMGT_FR4	TGGGGCCAAGGGACCACGGTCACCGTCTCCTCAG
10-D724-h5_VL		GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCATCCAGTTTGCAAAGTGGGGTCCCATCAAGGTTCAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGTCAACAGAGTTACAGTACCCCTCGGACGTTCGGCCAAGGGACCAAGGTGGAAATCAAACGAACTGTGGCTGCACCATCTGTCTTCATCTTCCCGCCATCTGATGAGCAGTTGAAATCTGGAACTGCCTCTGTTGTGTGCCTGCTGAATAACTTCTATCCCAGAGAGGCCAAAGTACAGTGGAAGGTGGATAACGCCCTCCAATCGGGTAACTCCCAGGAGAGTGTCACAGAGCAGGACAGCAAGGACAGCACCTACAGCCTCAGCAGCACCCTGACGCTGAGCAAAGCAGACTACGAGAAACACAAAGTCTACGCCTGCGAAGTCACCCATCAGGGCCTGAGCTCGCCCGTCACAAAGAGCTTCAACAGGGGAGAGTGT
	10-D724-h5_VL - IMGT_CDR1	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGCAGCTATTTAAATTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTATGCTGCATCCAGTTTGCAAAGT
	10-D724-h5_VL - IMGT_CDR2	AGGGCCAGC
	10-D724-h5_VL - IMGT_CDR3	CAACAGAGTTACAGTACCCCTCGGACG
	10-D724-h5_VL - IMGT_FR1	GACATCCAGATGACCCAGTCTCCATCCTCCCTGTCTGCATCTGTAGGAGACAGAGTCACCATCACTTGCCGGGCAAGTCAGAGCATTAGC
	10-D724-h5_VL - IMGT_FR2	CTGGCACTGGTATCAGCAGAAACCAGGGAAAGCCCCTAAGCTCCTGATCTAT
	10-D724-h5_VL - IMGT_FR3	AACCGTGCAGAGTCGGTCCCATCAGGTTCAGCGGCAGTGGATCTGGGACAGATTTCACTCTCACCATCAGCAGTCTGCAACCTGAAGATTTTGCAACTTACTACTGT
	10-D724-h5_VL - IMGT_FR4	TTCGGCCAAGGGACCAAGGTGGAAATCAAA

Table 37, Cont.



Name VH or VL	IMGT CDR and FR designation	Coding sequence of VH, VL FR and CDR
10-072446_VH		GAGGTGCAGCTGGTGGAGACCGGCGGAGGACTGGTGCAGCCTGGCAGGTCCCTGAGACTGTCCTGCGCCGCCTCCGGCTTCACCTTCGACGACTACGCCATGCACTGGGTCCGGCAGGCTCCAGGCAAGGGACTGGAATGGGTCTCCGGCATCACCTGGAACTCCGGCCACATCGACTACGCCGACTCCGTGGAGGGCCGGTTCACCATCTCCCGGGACAACGCCAAGAACTCCCTGTACCTGCAGATGAACTCCCTGAGAGCCGAGGACACCGCCGTGTACTACTGCGCCAAGGTGTCCTACCTGTCCACCGCCTCCAGCCTGGACTACTGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA
	10-072446_VH - IMGT_CDR1	GGCTTCACCTTCGACGACTACGCCATGCAC
	10-072446_VH - IMGT_CDR2	ATCACCTGGAACTCCGGCCACATCGAC
	10-072446_VH - IMGT_CDR3	GCCAAGGTGTCCTACCTGTCCACCGCCTCCAGCCTGGACTAC
	10-072446_VH - IMGT_FR1	GAGGTGCAGCTGGTGGAGACCGGCGGAGGACTGGTGCAGCCTGGCAGGTCCCTGAGACTGTCCTGCGCCGCCTCCGGCTTCACCTTC
	10-072446_VH - IMGT_FR2	TGGGAATGGGTCTCCGGCATCACCTGGAACTCCGGCCACATCGACTACGCCGACTCCGTGGAGGGCCGGTTCACC
	10-072446_VH - IMGT_FR3	ATCTCCCGGGACAACGCCAAGAACTCCCTGTACCTGCAGATGAACTCCCTGAGAGCCGAGGACACCGCCGTGTACTACTGC
	10-072446_VH - IMGT_FR4	TGGGGCCAGGGAACCCTGGTCACCGTCTCCTCA
10-072446_VL		GACATCCAGCTGACCCAGAGCCCTGCCAGCCTGAGCGCCAGCGTGGGCGAGACCGTGACCATCACCTGCCAGGCCAGCGAGAACATCTACGGCTTCCTGGCCTGGTATCAGCAGAAGCAGGGCAAGAGCCCCCAGCTGCTGATCTACGGCGCCAGCGACCTGGCCGACGGCGTGCCCAGCAGGTTCAGCGGCAGCGGCAGCGGCACCCAGTTCAGCCTGAAGATCAACAGCCTGCAGAGCGAGGACTTCGGCAGCTACTACTGCCAGAACGTGCTGAACACCCCCCTGACCTTCGGCGCCGGCACCAAGCTGGAGCTGAAG
	10-072446_VL - IMGT_CDR1	GAGAACATCTACGGCTTCCTGGCC
	10-072446_VL - IMGT_CDR2	GGCGCCAGC
	10-072446_VL - IMGT_CDR3	CAGGCCAGCGAGAACATCTACGTGAAC
	10-072446_VL - IMGT_FR1	GACATCCAGCTGACCCAGAGCCCTGCCAGCCTGAGCGCCAGCGTGGGCGAGACCGTGACCATCACCTGCCAGGCCAGC
	10-072446_VL - IMGT_FR2	CTGGCCTGGTATCAGCAGAAGCAGGGCAAGAGCCCCCAGCTGCTGATCTAC
	10-072446_VL - IMGT_FR3	AACGTGCTGAACACCCCCCTGACCTTCGGCGCCGGCACCAAGCTGGAGCTGAAG
	10-072446_VL - IMGT_FR4	TTCGGCGCCGGCACCAAGCTGGAGCTGAAG

Table 38: Exemplary amino acid sequences of human, crab-eating macaque, and dog P2RY8 proteins



Uniprot or NCBI Ref Seq ID	P2RY8 Protein	Sequence
Q86VZ1	Human P2RY8	MQVPNSTGPDNATQMLRNPAIAVAIPVVYSVAAVSIPGNLFSLWVLCRRMGPRSPSVIFMINLSVTDLMLASVIDFQIYHCNRHHWVFGVLLCNVTNVAFY AMMYSILTMTCISVERFLGVVYPLSSKRWRRRRYAVAACAGTWLLLTALSPLARTDLTYPVHALGITCDVLKWTMLDFSVAMWAVFLITFHLLFIIPVITVACYTA TILKLRTEEAHGREQRRAVGLAAVVLAFVTCFAPNNFVLLAHVSREYGKSYHAWYKLTDCLCLINNCLDPFVYFASREFQDRLRETLGCRVPRDTLDTRRESLF SARTTSVRSEAGAHPEGMEGATRPGLQRQESVF
XP_055555888	Crab-eating macaque (*Macaca fascicularis*) P2RY8	MEETGSSLPTHVPTLGPRGADPAATSPPAPLSRAPPPLQSPGEDPSRMHVPNSTGPDNATLQMLRNPTIAVALPVVYSVALVSIPGNLFSLWVLCRRGPKSPSVI FMINLSVTDLMLASVIDFQIYHCNRHHWVFGVLLCNVTVAFYAMMYSILTMTCISVERFLGVVYPLSSTRWRRRRYAVAACAGTWLLLAALSPLARTDLTYPV HALGITCDVLKWTMLDFSVAMWAVFLITFHLLFIIPVITVACYTATILKLRTEEAHGREQRRAVGLAVVVLAFVTCFAPNNFVLLAHVSREYGKSYHAWYKL TLCLSCINNCLDPFVYFASREFQDLRETLGCRVPRDPLDTRRESLSARTTSMRSSAGAHPEGLEGAPRPGLMRQESSF
XP_013867130	Dog P2RY8	MDAMNSGPDNATLMLRDPVIAVALPVVYSLVAVVSIPGNLFSLWVLCSHRGPKSPSVIFMINLSVTDLMLASVIDFQIYHNNGNHNWVFGEVLCNVTNVFYA NMMSSILTMTCISVERFLGVVYPLASAPWRRRRAYAACQAAWVLLLVALSPLARTDLTYAVEELGVTCDVLKSTMLPSVAMWAIFLTFHVLFHIPAVTVACYT ATILTLRASDPQGRCQRRRAVSLAFVVLLAFVTCFAPNNFVLLVHMAVSRDFLGRSYHAYYKLTLCLSCVNNCLDPFVYFASREFQDLRENLGVGPDPATCRDAGRD SLESPRTLSARSMASSGHEDGLEAPGRPALRRQESVF

Table 39: Exemplary amino acid sequence of a P2RY8 fusion protein comprising a human, crab-eating macaque, or dog P2RY8 and a mGFP fluorescent protein

P2RY8-mGFP Fusion Protein	Sequence
Human P2RY8 (UniProt ID: Q86VZ1) with C-terminal mGFP	MQVPNSTGPDNATLQMLRNPAIAVAIPVVYSLVAAVSIPGNLFSLWVLCRRMGPRSPSVIFMINLSVTDLMLASVIPFQIYYHCNRHHWVFGVLLCNVVTVAPY ANMYSSILTMTCISVERFLGVIYPLASKRWRRRIYAVAACAGTWILLTIALSPLARTDLTYPVHALGITCFDVLKWTMLPSVAMWAVFLFTIHILFLIPFVITVACYTA TILKLRTEEAHGREQRRRAVGLAAVVLLAPVTCFAPNNFVLLAHVSRLFYGKSYYAVYKLTLCLSCLNNCLDPFVYYFASREFQLRLREYLGCRIVPRDTLDTRRESLF SAIRTSVRSEAGAHPEGMEGATRPGLQRQESVFTRTRPPLEMSGGEELFAGIVPVLIELDGDVHGHKFSVRGEGEGDADYGKLEIKFICTTGKLPVPWPTLVTTLCYGI QCFARYPEHMKMNDFFKSAMPEGYIQERTIQFQDDGKYKTRGEVKFEGDTLVNRIELKGKDFKEDGNILGHKLEYSFNSHNVYIRPDKAINGLEANFKTRHNIEGG GVQLADHYQTNVPLGDGPVLLPINNHLSTQTKISKDPNEARDHMVLLEFSACCHTHGMDELYRSGLR*
Crab-eating macaque (Macaca fascicularis) P2RY8 (NCBI Ref Seq XP_005553888) with C-terminal mGFP	MEETGSSLPTHVPTLGPRGAIPAATSPPAPLSRAPPPLQSPGEDPSRMHVPNSTGPDNATLQMLRNPTIAVAIPVVYSLVAVSIPGNLFSLWVLCRRMGPKSPSVI FMINLSVTDLMLASVIPFQIYYHCNRNHWVFGVLLCNVVTVAPYANMYSSILTMTCISVERFLGVLYPLSSTRWRRRIYAVAACAGTWILLAALSPLARTDLTYPV HALGITCFDVLKWTMLPSVAMWAVFLFTIHILFLIPFVITVACYTATILKLRTEEAHGREQRRRAVGLAAVVLLAPVTCFAPNNFVLLAHVSRLFYGKSYYHVYKL TLCLSCLNNCLDPFVYYFASREFQLRLREYLGCRQVPGDPLDTRRESLFSAIRTSMRSEAGAHPEGLEGAPRPGLMRQESEFTRTRPTLEMSGGEELFAGIVPVLIELDGD VHGHKFSVRGEGEGDADYGKLEIKFICTTGKLPVPWPTLVTTLCYGIQCFARYPEHMKMNDFFKSAMPEGYIQERTIQFQDDGKYKTRGEVKFEGDTLVNRIELKGK DFKEDGNILGHKLEYSFNSHNVYIRPDKAINGLEANFKTRHNIEGGGVQLADHYQTNVPLGDGPVLLPINNHLSTQTKISKDPNEARDHMVLLEFSACCHTHGMD ELYRSGLR*
Dog P2RY8 (NCBI Ref Seq XP_013967139) with C-terminal mGFP tag	MDMNVSGPDNATLMLRDPVIAVAIPVVYSLVAAVSIPGNLFSLWVLCRHGPKSPSVIFMINLSVTDLMLASVIPFQIYYHRNGNHWVFGEVLCNVVTVWFYA NMYSSILTMTCISVERFLGVVYPLASAPWRRRNVAVAACAAWILLVALSPLARTDLTYAVEELGVTCDVLKSTMLPSVAMWAIFLFTIVLFFIPFVVTVACYT ATILTLDASDPQGRGQRRRAVSLAFVVLLAPVTCFAPNNFVLLVHAMVSRLFLGRSYYHVYKLTLCLSCVNNCLDPFVYYFASREFQLRLRMLGYGPLPATCRDAGRD SLESPRTLSARSMSSGHDGLEAPGRPALRRQESVFTRTRPLEMSGGEELFAGIVPVLIELDGDVHGHKFSVRGEGEGDADYGKLEIKFICTTGKLPVPWPTLVTTLCY GIQCFARYPEHMKMNDFFKSAMPEGYIQERTIQFQDDGKYKTRGEVKFEGDTLVNRIELKGKDFKEDGNILGHKLEYSFNSHNVYIRPDKAINGLEANFKTRHNIEG GGVQLADHYQTNVPLGDGPVLLPINNHLSTQTKISKDPNEARDHMVLLEFSACCHTHGMDELYRSGLR*

EXAMPLE 10: EFFICACY OF A HUMANIZED ANTI-P2RY8 ANTIBODY DRUG CONJUGATE, P2RY8-716-h3-ADC, IN INHIBITING OR REDUCING TUMOR GROWTH OR MASS OF P2RY8-POSITIVE CANCER CELL LINE XENOGRAFTS

[00274] This example demonstrates the efficacy of a humanized lead anti-P2RY8 antibody drug conjugate, P2RY8-716-h3 ADC, at inhibiting or reducing growth or mass of P2RY8-positive cancer cell line xenografts.

[00275] **P2RY8-716-h3-ADC**

[00276] The P2RY8-716-h3-ADC is a humanized P2RY8 antibody, P2RY8-716-h3, conjugated to 4 MMAEs at interchain thiols with a cleavable valine-citrulline-ρ-aminobenzyl (VC-PAB) linker.

[00277] **General methods for cell line xenograft studies**

[00278] Female SCID (CB17/Icr-Prkdcscid/IcrIcoCr) mice, 6-8 weeks old, purchased from Charles River Laboratories were used in this study. For the duration of this study, animals were housed in designated vivarium under the oversight of UCLA's Department of Laboratory Animal Medicine (DLAM). This is a fully approved AAALAC facility. All work was carried out under an Institutional Animal Care and Use Committee approved protocol. Animals were monitored daily by trained veterinarian staff from UCLA's Department of Laboratory Animal Medicine.

[00279] Animal health was assessed daily. In addition, mice were weighed 3 times per week and tumor volumes were measured 3 times per week. Standard housing practices were used with 4-5 animals per cage without restraint and full access to food and water. Facilities were monitored daily by the DLAM veterinary staff.

[00280] Tumor xenografts were measured with calipers thrice a week, and tumor volume in mm3 was determined by multiplying height × width × length. Mouse body weights were recorded three times per week. Animals were euthanized at end of study and tumor tissue was excised and divided to be stored as snap-frozen or formalin fixed paraffin embedded (FFPE) tissue.

[00281] End points for each study were >10% body weight loss or a tumor volume that impairs ambulation of the animal or a tumor that becomes ulcerated. End of study, after three cycles of treatment followed by recovery phase was also a termination point.

[00282] **Results**

[00283] The results of the xenograft studies assessing efficacy of P2RY8-716-h3-ADC are shown in Figures 17-22.

[00284] Figure 17 shows the efficacy of P2RY8-ADC in P2RY8-positive SUDHL-10 lymphoma cell line xenografts with IVIG pre-treatment. A-C) SUDHL-10 (lymphoma) cell line xenografts were injected into SCID mice at 10 million cells per mouse. Once tumors reached a volume of 250-300 mm^3, mice were randomized into treatment groups. Prior to initiation of treatment, each mouse received an IV tail vein injection of 10 mg/kg human immunoglobulin (IVIG) with the aim of reducing non-specific binding of the ADCs to Fc receptors on tumor associated macrophages (TAMs). IVIG treatments were given 24 hours before each dose of ADC or control mAb. For treatments, Mice were dosed with control non-targeting human IgG antibody (Hu-IgG Control mAb) or P2RY8-targeting ADC (P2RY8-716-h3-ADC) or a non-targeting humanized IgG control ADC (Hu-IgG Control ADC) at the doses indicated by IV tail vein injection. Mice received three once weekly (QW) treatments. Lines represent mean tumor volume ± SEM. 6 mice per arm. B) Bar charts represent mean change in xenograft tumor volume between the start of treatment and the last day of measurement of the Hu-IgG Control mAb (volume at day 1 minus volume at day 23). C) No significant impact on mouse body weights were observed during the treatment window.

[00285] Figure 18 shows the efficacy of P2RY8-ADC in P2RY8-positive SUDHL-5 lymphoma cell line xenografts with IVIG pre-treatment. A-C) SUDHL-5 (lymphoma) cell line xenografts were injected into SCID mice at 5 million cells per mouse. Once tumors reached a volume of 350 -400 mm^3, mice were randomized into treatment groups and pre-treated with IVIG 24 hours before prior to treatment with either control non-targeting human IgG antibody (Hu-IgG Control mAb) or P2RY8-targeting ADC (P2RY8-716-h3-ADC) or a non-targeting humanized IgG control ADC (Hu-IgG Control ADC) at the doses indicated by IV tail vein injection. Line represents mean tumor volume ± SEM 6 mice per arm Bar charts represent mean change in xenograft tumor volume between the start of treatment and the last day of measurement of the Hu-IgG Control mAb (volume at day 1 minus volume at day 11). No significant impact on mouse body weights were observed during the treatment window.

[00286] Figure 19 shows the efficacy of P2RY8-ADC in P2RY8-positive RL lymphoma cell line xenografts. A-C) RL (lymphoma) cell line xenografts were injected into SCID mice at 1 million cells per mouse. Once tumors reached a volume of 150-200 mm^3, mice were randomized into treatment groups and treated with control non-targeting human IgG antibody (Hu-IgG) or P2RY8-targeting ADC (P2RY8-716-h3-ADC) or a non-targeting

humanized IgG control ADC (Hu-IgG Control ADC) at the doses indicated by IV tail vein injection. 6 mice per arm. Line represents mean tumor volume ± SEM. Bar charts represent mean change in xenograft tumor volume (volume at day 1 minus volume at day 24).

[00287] Figure 20 shows the lack of efficacy of the P2RY8-ADC in P2RY8-negative SCC-3 lymphoma cell line xenografts. A-C) SCC-3 (lymphoma) cell line xenografts were injected into SCID mice at 5 million cells per mouse. Once tumors reached a volume of 200-300 mm^3, mice were randomized into treatment groups and treated with control non-targeting human IgG antibody (Hu-IgG) or P2RY8-targeting ADC (P2RY8-716-h3-ADC) or a non-targeting humanized IgG control ADC (Hu-IgG Control ADC) at the doses indicated by IV tail vein injection. 6 mice per arm. Line represents mean tumor volume ± SEM. Bar charts represent mean change in xenograft tumor volume (volume at day 1 minus volume at day 16).

[00288] Figure 21 shows the efficacy of P2RY8-ADC in P2RY8-positive SUDHL-10 lymphoma cell line xenografts in the absence of IVIG pre-treatment. A-C) SUDHL-10 (lymphoma) cell line xenografts were injected into SCID mice at 10 million cells per mouse. Once tumors reached a volume of 200-250 mm^3, mice were randomized into treatment groups and dosed with control non-targeting human IgG antibody (Hu-IgG Control mAb) or P2RY8-targeting ADC (P2RY8-716-h3-ADC) or a non-targeting humanized IgG control ADC (Hu-IgG Control ADC) at the doses indicated by IV tail vein injection. Mice received three once weekly (QW) treatments. Lines represent mean tumor volume ± SEM. 6 mice per arm. B) Bar charts represent mean change in xenograft tumor volume between the start of treatment and the last day of measurement of the Hu-IgG Control mAb (volume at day 1 minus volume at day 21). C) No significant impact on mouse body weights were observed during the treatment window.

[00289] Figure 22 shows the efficacy of P2RY8-ADC in P2RY8-positive SUDHL-5 lymphoma cell line xenografts in the absence of IVIG pre-treatment. A-C) SUDHL-5 (lymphoma) cell line xenografts were injected into SCID mice at 5 million cells per mouse. Once tumors reached a volume of 200-250 mm^3, mice were randomized into treatment groups and dosed with control non-targeting human IgG antibody (Hu-IgG Control mAb) or P2RY8-targeting ADC (P2RY8-716-h3-ADC) or a non-targeting humanized IgG control ADC (Hu-IgG Control ADC) at the doses indicated by IV tail vein injection. Mice received three once weekly (QW) treatments. Lines represent mean tumor volume ± SEM. 6 mice per arm. B) Bar charts represent mean change in xenograft tumor volume between the start

of treatment and the last day of measurement of the Hu-IgG Control mAb (volume at day 1 minus volume at day 20). C) No significant impact on mouse body weights were observed during the treatment window.

[00290] The single-agent activity of a P2RY8-ADC was assessed in cell line xenograft models of human lymphoma, previously determined by flow cytometry as either positive (P2RY8+) or negative (P2RY8-), for cell surface P2RY8 protein; SUDHL-5 (P2RY8+), SUDHL-10 (P2RY8+), RL (P2RY8+), and SCC-3 (P2RY8-). The P2RY8-targeting ADC, P2RY8-716-h3-ADC, showed selective activity in P2RY8 positive cell line xenografts. Xenograft tumor growth regressions were observed in response to treatment with P2RY8-716-h3-ADC in the three P2RY8+ models (Figures 17-19, 21 and 22). Non-specific activity of the Hu-IgG Control ADC was observed in two of the P2RY8+ models (Figures 21 and 22). This activity in the control arm is likely due to uptake of the Hu-IgG Control ADC into these tumor cells by tumor associated macrophages (TAMs).

[00291] To address this, we repeated these studies with pre-treatments of human immunoglobulin (IVIG) to mop up the Fc receptors on the TAMs. Under these conditions, activity of P2RY8-716-h3-ADC is clearly distinct from the Hu-IgG Control ADC (Figures 17 and 19). No anti-tumor activity was observed in the P2RY8- SCC-3 cell line xenografts in response to treatment with P2RY8-716-h3-ADC, indicating that activity of the ADC is likely to be restricted to cancers that express the target.

[00292] These data show that the humanized P2RY8-ADC, P2RY8-716-h3-ADC, has potent, selective anti-tumor activity in P2RY8+ models of human lymphomas.

[00293] All references, including Uniprot designations, publications, patent applications, and patents, cited herein are hereby incorporated by reference to the same extent as if each reference were individually and specifically indicated to be incorporated by reference and were set forth in its entirety herein.

[00294] The use of the terms “a” and “an” and “the” and similar referents in the context of describing the disclosure (especially in the context of the following claims) are to be construed to cover both the singular and the plural, unless otherwise indicated herein or clearly contradicted by context. The terms “comprising,” “having,” “including,” and “containing” are to be construed as open-ended terms (i.e., meaning “including, but not limited to,”) unless otherwise noted.

[00295] The use of the term “about” as used herein when referring to a measurable value such as an amount of a compound or agent of this invention, dose, time, temperature, and

the like, is meant to encompass variations of ± 10%, ± 5%, ± 1%, ± 0.5%, or even ± 0.1% of the specified amount. For sequence identity, "about" as used for percent sequence identity encompasses variations of ± 5%. Unless otherwise indicated, all numbers expressing quantities of ingredients, properties such as reaction conditions, and so forth used in the specification and claims are to be understood as being modified in all instances by the term "about."

[00296] Recitation of ranges of values herein are merely intended to serve as a shorthand method of referring individually to each separate value falling within the range and each endpoint, unless otherwise indicated herein, and each separate value and endpoint is incorporated into the specification as if it were individually recited herein.

[00297] All methods described herein can be performed in any suitable order unless otherwise indicated herein or otherwise clearly contradicted by context. The use of any and all examples, or various language (e.g., "such as") provided herein, is intended merely to better illuminate the disclosure and does not pose a limitation on the scope of the disclosure unless otherwise claimed. No language in the specification should be construed as indicating any non-claimed element as essential to the practice of the disclosure.

[00298] Variations of the embodiments of present disclosure may become apparent to those of ordinary skill in the art upon reading the foregoing description. The inventors expect skilled artisans to employ such variations as appropriate, and the inventors intend for the disclosure to be practiced otherwise than as specifically described herein. Accordingly, this disclosure includes all modifications and equivalents of the subject matter recited in the claims appended hereto as permitted by applicable law. Moreover, any combination of the above-described elements in all possible variations thereof is encompassed by the disclosure unless otherwise indicated herein or otherwise clearly contradicted by context.

WHAT IS CLAIMED IS:

1. An antigen-binding protein comprising:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 177)
or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK
PGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFA
TYYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

2. The antigen-binding protein of claim 1 comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of:
GYSITSDYA (SEQ ID NO: 178) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(b) a heavy chain CDR2 comprising the amino acid sequence of:
ITYSGTT (SEQ ID NO: 179) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(c) a heavy chain CDR3 comprising the amino acid sequence of:
ARGYWYFDV (SEQ ID NO: 180) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(d) a light chain CDR1 comprising the amino acid sequence of:
ESVDSYGYTF (SEQ ID NO: 186) or a variant sequence thereof which differs by only one or two amino acids or which has at least or

about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 187) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 188) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

3. An antigen-binding protein comprising:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK
PGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFA
TYYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

4. An antigen-binding protein comprising

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 161)

or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKP GKAPKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATY YCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 169) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

5. An antigen-binding protein comprising:
(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKP GKAPKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATY YCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 201) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

6. An antigen-binding protein comprising:
(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only one or two amino

acids or which has at least or about 85% sequence identity; and/or
(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK
PGKAPKLLIYRASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFAT
YYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

7. An antigen-binding protein comprising:
(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKP
GKAPKLLIYRASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATY
YCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 233) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

8. An antigen-binding protein comprising:
(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWMGYITYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAPKLLIY RASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDPFTFGQGTKL EIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

9. An antigen-binding protein comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 146) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 147) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 148) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 154) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 155) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 156) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

10. An antigen-binding protein comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 162) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 163) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 164) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 170) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 171) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 172) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

11. An antigen-binding protein comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 194) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of:

ITYSGTT (SEQ ID NO: 195) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 196) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 202) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 203) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 204) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

12. An antigen-binding protein comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 210) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 211) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 212) or a variant sequence thereof which differs by only one or two amino acids or which has at least or

about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 218) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 219) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 220) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

13. An antigen-binding protein comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 226) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 227) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 228) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO:234) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS

(SEQ ID NO: 235) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 236) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

14. An antigen-binding protein comprising:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 242) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 243) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 244) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 250) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 251) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 252) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about

70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

15. The antigen-binding protein of claim 9, additionally comprising:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 149) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 150) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 151) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 152) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 157) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 158) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 159) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence

identity;

(h) a light chain FR4 comprising the amino acid sequence: FGQGTKLEIK (SEQ ID NO: 160) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or more of (a)-(h).

16. The antigen-binding protein of claim 10, additionally comprising:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 165) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 166) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 167) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 168) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 173) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 174) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 175) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 comprising the amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 176) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or more of (a)-(h).

17. The antigen-binding protein of claim 2, additionally comprising:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 181) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 182) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 183) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 184) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 189) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 190) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 191) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 192) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or
(i) a combination of any two or more of (a)-(h).

18. The antigen-binding protein of claim 11, additionally comprising:
(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 197) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 198) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 199) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 200) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 205) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 206) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 207) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 208) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or
(i) a combination of any two or more of (a)-(h).

19. The antigen-binding protein of claim 12, additionally comprising:
(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 213) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 214) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 215) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 216) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 221) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 222) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYC (SEQ ID NO: 223) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 224) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or
(i) a combination of any two or more of (a)-(h).

20. The antigen-binding protein of claim 13, additionally comprising:
(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 229) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 230) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(c) a heavy chain FR3 comprising the amino acid sequence:

TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 231) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 232) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 237) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 238) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC (SEQ ID NO: 239) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 240) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or more of (a)-(h).

21. The antigen-binding protein of claim 14, additionally comprising:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 245) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence of:

WNWIRQAPGKGLEWMGY (SEQ ID NO: 246) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(c) a heavy chain FR3 comprising the amino acid sequence: TYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 247) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 248) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 253) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 254) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 255) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 256) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or
(i) a combination of any two or more of (a)-(h).

22. An antigen-binding protein comprising:
(a) a heavy chain variable region having the amino acid sequence of:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 145)
or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK
PGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFA
TYYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

23. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWVSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 161)
or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKP
GKAPKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATY
YCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 169) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

24. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG
KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR
AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 177)

or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK PGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFA TYYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

25. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKP GKAPKLLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATY YCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 201) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

26. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK PGKAPKLLIYRASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFAT YYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

27. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG KGLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVR AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKP GKAPKLLIYRASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATY YCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 233) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

28. An antigen-binding protein comprising:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPG KGLEWMGYITYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVR AEDTAVYYCARGYWYFDVWGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQK PGKAPKLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFA

TYYCQQSNEDPFTFGQGTKLEIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

29. The antigen-binding protein of any one of the previous claims, wherein the variant sequence has at least about 80% or at least or about 85% sequence identity.

30. The antigen-binding protein of any one of the previous claims, wherein the variant sequence has at least about 90% sequence identity or at least or about 95% sequence identity.

31. The antigen-binding protein of claim of any one of the previous claims, wherein:

(a) the antigen-binding protein binds to a human P2Y receptor family member 8 (P2RY8) protein (SEQ ID NO: 369);

(b) the antigen-binding protein binds an extracellular domain of human P2RY8 with a dissociation constant (K_D) of about less than 10 nM, 5 nM, 2.5 nM, 1 nM, 0.5 nM or 0.25 nM;

(c) the antigen-binding protein preferentially binds human P2RY8 over dog P2RY8 (SEQ ID NO: 371);

(d) the antigen-binding protein does not bind dog P2RY8; or

(e) any combination thereof.

32. The antigen-binding protein of claim 31, wherein the human P2RY8 (SEQ ID NO: 369) is expressed on the surface of a cell; the dog P2RY8 (SEQ ID NO: 371) is expressed on the surface of a cell; and the antigen-binding protein preferentially binds the human P2RY8 over dog P2RY8 by a factor of at least about 10x, 20x, 30x, 50x, 75x, 100x, 125x, 150x, 175x, 200x, 225x, 250x, 275x, 300x, or 325x.

33. The antigen-binding protein of any one of the previous claims, which is an antibody or antigen-binding antibody fragment.

34. The antigen-binding protein of claim 33, wherein the antibody is a monoclonal antibody.

35. The antigen-binding protein of claim 33 or 34, wherein the antibody is a human or humanized antibody.

36. The antigen-binding protein of any one of claims 33-35, which is an IgG.

37. The antigen-binding protein of claim 36, wherein the IgG is selected from the group consisting of IgG1, IgG2, IgG3, and IgG4.

38. The antigen-binding protein of claim 36 or 37, wherein the IgG is IgG1.

39. The antigen-binding protein of claim 33, wherein the antigen-binding antibody fragment is selected from the group consisting of scFv, $F(ab')_2$, Fab, Fab', and Fv.

40. The antigen-binding protein of any one of the previous claims, which inhibits tumor growth in xenograft mice injected with human cancer cells.

41. The antigen-binding protein of any one of the previous claims, wherein the antigen-binding protein comprises (a) an Fc polypeptide, or (b) an Fc polypeptide comprising an afucosylated glycan.

42. A conjugate comprising an antigen-binding protein of any one of the previous claims or those described herein, or an antigen-binding fragment thereof.

43. The conjugate of claim 42 comprising a cytotoxic agent or a chemotherapeutic agent.

44. The conjugate of claim 43, wherein the chemotherapeutic agent is an anti-mitotic agent which inhibits cell division by blocking tubulin polymerization.

45. The conjugate of claim 44, wherein the anti-mitotic agent is an auristatin.

46. The conjugate of claim 45, wherein the auristatin is monomethyl auristatin E (MMAE).

47. The conjugate of any one of claims 43-46, wherein the agent is conjugated to the antigen-binding protein via a cleavable linker.

48. The conjugate of claim 47, wherein the cleavable linker is VC-PAB.

49. The conjugate of any one of claims 42-48, wherein the antigen-binding protein is an antibody.

50. The conjugate of claim 49, wherein the antibody is a monoclonal antibody.

51. The conjugate of claim 49 or 50, wherein the antibody is a human antibody, humanized antibody, or a chimeric antibody.

52. The conjugate of any one of claims 49-51, wherein the antibody is an IgG antibody, optionally wherein the IgG is IgG1.

53. The conjugate of any one of claims 42-52, wherein an average number of units of an agent conjugated per antigen-binding protein is in a range of 1 to 8, preferably wherein the average number of units of an agent conjugated per antigen-binding protein is in a range of 3-8.

54. The conjugate of any one of claims 42-53, wherein the conjugate is a heterogeneous conjugate.

55. The conjugate of any one of claims 42-53, wherein the conjugate is a homogeneous conjugate.

56. The conjugate of any one of claims 42-55, wherein an agent is conjugated at a specific site of the antigen-binding protein.

57. The conjugate of claim 56, wherein the specific site is an unpaired cysteine residue.

58. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 145 and SEQ ID NO: 153 conjugated to VC-PAB-MMAE.

59. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 161 and SEQ ID NO: 169 conjugated to VC-PAB-MMAE.

60. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 177 and SEQ ID NO: 185 conjugated to VC-PAB-MMAE.

61. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 193 and SEQ ID NO: 201 conjugated to VC-PAB-MMAE.

62. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 209 and SEQ ID NO: 217 conjugated to VC-PAB-MMAE.

63. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 225 and SEQ ID NO: 233 conjugated to VC-PAB-MMAE.

64. The conjugate of any one of claims 42-57, wherein the conjugate comprises a polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 241 and SEQ ID NO: 249 conjugated to VC-PAB-MMAE.

65. A bispecific antigen-binding protein comprising the antigen-binding protein of any one of claims 1-41, an antigen binding protein of Table 3, or a fragment thereof that binds to a human P2Y receptor family member 8 (P2RY8) protein (SEQ ID NO: 369) and a second antigen-binding protein that binds a second antigen.

66. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW
MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR
GYWYFDVWGQGTTVTVSS (SEQ ID NO: 177) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP
KLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDP
FTFGQGTKLEIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

67. The bispecific antigen-binding protein of claim 66, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 178) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 179) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 180) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 186) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID

NO: 187) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 188) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

68. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW VSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

69. The bispecific antigen-binding protein of claim 68, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 146) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 147) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of:

ARGYWYFDV (SEQ ID NO: 148) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 154) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 155) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 156) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

70. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW VSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 161) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPK LLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPF TFGQGTKLEIK (SEQ ID NO: 169) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

71. The bispecific antigen-binding protein of claim 70, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 162) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 163) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 164) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 170) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 171) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;
(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 172) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or
(g) a combination of any two or moreof (a)-(f).

72. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPK LLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPF TFGQGTKLEIK (SEQ ID NO: 201) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

73. The bispecific antigen-binding protein of claim 72, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 194) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 195) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 196) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 202) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 203) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 204) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

74. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

75. The bispecific antigen-binding protein of claim 74, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 210) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 211) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 212) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 218) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 219) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 220) or a variant sequence thereof which differs by only one or

two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or more of (a)-(f).

76. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPK LLIYRASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPF TFGQGTKLEIK (SEQ ID NO: 233) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

77. The bispecific antigen-binding protein of claim 76, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 226) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT (SEQ ID NO: 227) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 228) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF

(SEQ ID NO:234) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 235) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 236) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

78. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCA RGYWYFDVWGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(b) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

79. The bispecific antigen-binding protein of claim 78, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain CDR1 comprising the amino acid sequence of: GYSITSDYA (SEQ ID NO: 242) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(b) a heavy chain CDR2 comprising the amino acid sequence of: ITYSGTT

(SEQ ID NO: 243) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(c) a heavy chain CDR3 comprising the amino acid sequence of: ARGYWYFDV (SEQ ID NO: 244) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(d) a light chain CDR1 comprising the amino acid sequence of: ESVDSYGYTF (SEQ ID NO: 250) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(e) a light chain CDR2 comprising the amino acid sequence of: RAS (SEQ ID NO: 251) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity;

(f) a light chain CDR3 comprising the amino acid sequence of: QQSNEDPFT (SEQ ID NO: 252) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 70% sequence identity; or

(g) a combination of any two or moreof (a)-(f).

80. The bispecific antigen-binding protein of claim 66, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 181) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 182) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 183) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 184) or a variant sequence thereof which differs by only one or

two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 189) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 190) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 191) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 192) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or more of (a)-(h).

81. The bispecific antigen-binding protein of claim 68, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 149) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 150) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 151) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 152) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 157) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 158) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 159) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 comprising the amino acid sequence: FGQGTKLEIK (SEQ ID NO: 160) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or moreof (a)-(h).

82. The bispecific antigen-binding protein of claim 70, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 165) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence: WNWIRQAPGKGLEWVSY (SEQ ID NO: 166) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence:

TYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYC (SEQ ID NO: 167) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 168) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 173) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 174) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 175) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 comprising the amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 176) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or more of (a)-(h).

83. The bispecific antigen-binding protein of claim 72, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 197) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 198) or a variant sequence thereof

which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 199) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 200) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 205) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 206) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC (SEQ ID NO: 207) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 208) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or moreof (a)-(h).

84. The bispecific antigen-binding protein of claim 74, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 213) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 214) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 215) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 216) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 221) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 222) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYC (SEQ ID NO: 223) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 224) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or moreof (a)-(h).

85. The bispecific antigen-binding protein of claim 76, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 229) or a variant

sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 230) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(c) a heavy chain FR3 comprising the amino acid sequence: TYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 231) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 232) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(e) a light chain FR1 comprising the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRAS (SEQ ID NO: 237) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 238) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(g) a light chain FR3 comprising the amino acid sequence: NVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC (SEQ ID NO: 239) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;

(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 240) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or

(i) a combination of any two or moreof (a)-(h).

86. The bispecific antigen-binding protein of claim 78, wherein the antigen-binding protein that binds to the P2RY8 protein additionally comprises:

(a) a heavy chain FR1 comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVS (SEQ ID NO: 245) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(b) a heavy chain FR2 comprising the amino acid sequence of: WNWIRQAPGKGLEWMGY (SEQ ID NO: 246) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(c) a heavy chain FR3 comprising the amino acid sequence: TYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYC (SEQ ID NO: 247) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(d) a heavy chain FR4 comprising the amino acid sequence: WGQGTTVTVSS (SEQ ID NO: 248) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(e) a light chain FR1 comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRAS (SEQ ID NO: 253) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(f) a light chain FR2 comprising the amino acid sequence: MHWYQQKPGKAPKLLIY (SEQ ID NO: 254) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(g) a light chain FR3 comprising the amino acid sequence: NVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC (SEQ ID NO: 255) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity;
(h) a light chain FR4 amino acid sequence of: FGQGTKLEIK (SEQ ID NO: 256) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85%, 90% or 95% sequence identity; or
(i) a combination of any two or moreof (a)-(h).

87. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 177) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 185) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

88. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence of: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW VSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 145) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 153) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

89. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence:

EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW VSYITYSGTTTYNPSLKSRFTISRDTSKNTFYLQMNSLRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 161) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPK LLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPF TFGQGTKLEIK (SEQ ID NO: 169) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

90. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 193) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPK LLIYRASNVESGIPSRFSGSGSGTDFTLTISSVQPEDFATYYCQQSNEDPF TFGQGTKLEIK (SEQ ID NO: 201) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

91. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 209) or a variant sequence thereof

which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSRTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 217) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

92. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAEDTAVYYCAR GYWYFDVWGQGTTVTVSS (SEQ ID NO: 225) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDSYGYTFMHWYQQKPGKAPK LLIYRASNVESGIPSRFSGSGSRTDFTLTISSVQPEDFATYYCQQSNEDPF TFGQGTKLEIK (SEQ ID NO: 233) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

93. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein comprises:

(a) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGKGLEW MGYITYSGTTTYADSLKGRITISRDTSKNTFYLQLNSVRAEDTAVYYCA RGYWYFDVWGQGTTVTVSS (SEQ ID NO: 241) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(b) a light chain variable region having the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASESVDSYGYTFMHWYQQKPGKAP KLLIYRASNVESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSNEDP FTFGQGTKLEIK (SEQ ID NO: 249) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity.

94. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein is selected from the group consisting of:

(a) an antigen-binding protein comprising:

(i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 257) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKP GKAPKLLIYRASNVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATY YCQQSNEDLLTFGQGTKLEIK (SEQ ID NO: 265) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity;

(b) an antigen-binding protein comprising:

(i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 273) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:

DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPG
KAPKLLIYRASNVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC
QQSNEDLLTFGQGTKLEIK (SEQ ID NO: 281) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity;

(c) an antigen-binding protein comprising:
(i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK
GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE
DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 289) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKP
GKAPKLLIYRASNVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATY
YCQQSNEDLLTFGQGTKLEIK (SEQ ID NO: 297) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and

(d) an antigen-binding protein comprising:
(i) CDR1-3 derived from a heavy chain variable region comprising the amino acid sequence:
EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK
GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE
DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 305) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(ii) CDR1-3 derived from a light chain variable region comprising the amino acid sequence:
DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPG
KAPKLLIYRASNVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC
QQSNEDLLTFGQGTKLEIK (SEQ ID NO: 313) or a variant sequence

thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

95. The bispecific antigen-binding protein of claim 65, wherein the antigen-binding protein that binds to the P2RY8 protein is selected from the group consisting of:

(a) an antigen-binding protein comprising:

(i) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 257) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity; and/or

(ii) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKP GKAPKLLIYRASNVQSGVPSRFSGSGSGTDFTLTISSLQPEDFATY YCQQSNEDLLTFGQGTKLEIK (SEQ ID NO: 265) or a variant sequence thereof which differs by only 1-5 amino acids or which has at least or about 85%, 90%, 95%, 98% or 99% sequence identity;

(b) an antigen-binding protein comprising:

(i) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 273) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or

(ii) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPG KAPKLLIYRASNVQSGIPSRFSGSGSGTDFTLTISSVQPEDFATYYC QQSNEDLLTFGQGTKLEIK (SEQ ID NO: 281) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity;

(c) an antigen-binding protein comprising:

(i) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 289) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(ii) a light chain variable region having the amino acid sequence: DIQMTQSPSSLSASVGDRVTITCRASESVDTYGYNFLHWYQQKP GKAPKLLIYRASNVQSGVPSRFSGSGSRTDFTLTISSLQPEDFATY YCQQSNEDLLTFGQGTKLEIK (SEQ ID NO: 297) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and

(d) an antigen-binding protein comprising:
(i) a heavy chain variable region having the amino acid sequence: EVQLVESGGGLVQPGGSLRLSCAVSGYSITSDYAWNWIRQAPGK GLEWMGYITYSGTTTYNPSLKSRITISRDTSKNTFYLQLNSVRAE DTAVYYCARGFWYFDVWGQGTTVTVSS (SEQ ID NO: 305) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity; and/or
(ii) a light chain variable region having the amino acid sequence: DIQLTQSPSSLSASVGDRATITCRASESVDTYGYNFLHWYQQKPG KAPKLLIYRASNVQSGIPSRFSGSGSRTDFTLTISSVQPEDFATYYC QQSNEDLLTFGQGTKLEIK (SEQ ID NO: 313) or a variant sequence thereof which differs by only one or two amino acids or which has at least or about 85% sequence identity.

96. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is a cell surface protein expressed by a T-cell, optionally, a component of the T-cell receptor (TCR), for example, CD3.

97. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is a costimulatory molecule which assists in T-cell activation, e.g., CD40 or 4-lBB (CD137).

98. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is an Fc receptor, optionally, a Fc gamma receptor, Fc-alpha receptor, or Fc-epsilon receptor.

99. The bispecific antigen-binding protein of claim 98, wherein the Fc receptor is CD64 (Fc-gamma RI), CD32 (Fc-gamma RIIA), CD16A (Fc-gamma RIIIA), CD16b (Fc-gamma RIIIb), FcεRI, CD23 (Fc-epsilon RII), CD89 (Fc-epsilon RI), Fcα/μR, or FcRn.

100. The bispecific antigen-binding protein of claim 98 or 99, wherein the Fc receptor is CD16A.

101. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is an immune checkpoint molecule, e.g., a protein involved in the immune checkpoint pathway, optionally, A2AR, B7-H3, B7-H4, BTLA, CTLA4, IDO, KIR, LAG3, NOX2, PD-1, TIM3, VISTA, or SIGLEC7.

102. The bispecific antigen-binding protein of claim 101, wherein the immune checkpoint molecule is PD-1, LAG3, TIM3, or CTLA4.

103. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is CD3.

104. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is CD3E.

105. The bispecific antigen-binding protein of any one of claims 65-95, wherein the second antigen is CD16A.

106. The bispecific antigen-binding protein of any one of claims 65-105, comprising an scFv, a Fab, or a $F(ab')_2$ of any of the presently disclosed P2RY8 antibodies.

107. The bispecific antigen-binding protein of any one of claims 65-106, comprising a structure of a nanobody, BiTE®, DART, TandAb, CrossMab, or HSAbody.

108. A fusion protein comprising an antigen-binding protein of any one of the previous claims or those described herein, or an antigen-binding fragment thereof.

109. A nucleic acid comprising a nucleotide sequence encoding the antigen binding protein of any one of claims 1-41, the bispecific antigen-binding protein of any one of claims 65-107, or the fusion protein of claim 108.

110. The nucleic acid of claim 109, wherein the nucleic acid is a complementary DNA (cDNA).

111. A vector comprising the nucleic acid of claim 109 or 110.

112. The vector of claim 111, additionally comprising an internal ribosome entry site (IRES).

113. A host cell comprising the nucleic acid of claim 109, the cDNA of claim 110, or the vector of claim 111 or 112.

114. The host cell of claim 113, wherein the host cell is a bacterial cell.

115. The host cell of claim 113, wherein the host cell is a eukaryotic cell.

116. The host cell of claim 113 or 115, wherein the host cell is a mammalian cell.

117. The host cell of claim 116, wherein the mammalian cell is a Chinese hamster ovary (CHO) cell.

118. A method of producing an antigen-binding protein that binds to a P2Y receptor family member 8 (P2RY8) protein, comprising (i) culturing the host cell of any one of claims 113-117 in a cell culture medium, and (ii) harvesting the antigen-binding protein from the cell culture medium.

119. A method of producing a bispecific antigen-binding protein comprising an antigen-binding protein that binds to a P2Y receptor family member 8 (P2RY8) protein, comprising (i) culturing the host cell of any one of claims 113-117 in a cell culture medium, and (ii) harvesting the bispecific antigen-binding protein from the cell culture medium.

120. A method of producing a fusion protein comprising an antigen-binding protein that binds to a P2Y receptor family member 8 (P2RY8) protein, comprising (i) culturing the host cell of any one of claims 113-117 in a cell culture medium, and (ii) harvesting the fusion protein from the cell culture medium.

121. A method of producing a pharmaceutical composition comprising combining the antigen-binding protein of any one of claims 1-41, the conjugate of any one of claims 42-64, the bispecific antigen-binding protein of any one of claims 65-107, the fusion protein of claim 108, the nucleic acid of claim 109 or 110, the vector of claim 111 or 112, the host cell of any one of claims 113-117, or a combination thereof; and a pharmaceutically acceptable carrier, diluent, or excipient.

122. A pharmaceutical composition comprising the antigen-binding protein of any one of claims 1-41, the conjugate of any one of claims 42-64, the bispecific antigen-binding protein of any one of claims 65-107, the fusion protein of claim 108, the nucleic acid of claim 109 or 110, the vector of claim 111 or 112, the host cell of claim any one of claims 113-117, or a combination thereof; and a pharmaceutically acceptable carrier, diluent, or excipient.

123. A method of treating a subject with a P2RY8-expressing cancer comprising administering to the subject the pharmaceutical composition of claim 122 in an amount effective to treat the cancer.

124. A method of inhibiting tumor growth in a subject, comprising administering to the subject the pharmaceutical composition of claim 122 in an amount effective to inhibit tumor growth.

125. A method of reducing tumor size in a subject, comprising administering to the subject the pharmaceutical composition of claim 122 in an amount effective to reduce tumor size.

126. A method of preventing the recurrence of cancer in a subject, comprising administering to the subject the pharmaceutical composition of claim 122 in an amount effective to prevent the recurrence of cancer.

127. The method of any one of claims123-126, wherein the pharmaceutical composition induces apoptosis in tumor cells.

128. The method of any one of claims 123-126, wherein the pharmaceutical composition induces apoptosis in cells expressing P2RY8.

129. A method of detecting the P2Y receptor family member 8 (P2RY8) protein or a fragment thereof in a sample, comprising contacting the sample with the antigen-binding protein of any one of claims 1-41, the conjugate of any one of claims 42-64, the bispecific antigen-binding protein of any one of claims 65-107, or the fusion protein of claim 108, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate, or fusion protein bound to the P2RY8 protein or a fragment thereof.

130. A method of diagnosing a P2Y receptor family member 8 (P2RY8) protein-positive cancer in a subject, comprising contacting a sample (e.g., biological sample comprising cells or tissue) from the subject with the antigen-binding protein of any one of claims 1-41, the conjugate of any one of claims 42-64, the bispecific antigen-binding protein of any one of claims 65-107, or the fusion protein of claim 108, and assaying for an immunocomplex comprising the antigen-binding protein, conjugate, or fusion protein bound to the P2RY8 protein or a fragment thereof.